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THE OPHTHALMO-REACTION IN TYPHOID FEVER.

By Charles R. Austrian, M. D.

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(From the Medical Clinic of the Johns Hopkins Hospital.)

When Calmette published his article on the ophthalmo-reaction in tuberculosis, clinicians welcomed the method as a valuable diagnostic aid and subsequent studies have shown that the welcome given it was no more hearty than it merited. The possibility of employing a like procedure in the diagnosis of other diseases was at once apparent. In typhoid fever, for instance, it was readily appreciated that if an eye test which was reliable could be devised, it would offer the advantages of being a bedside test, made and interpreted by the physician and unattended by discomfort to the patient.

Chantemesse[1] was the first to realize these facts, and in 1907 he described an "Ophthalmo-diagnostic" for typhoid fever. The method he employed was as follows: The twenty-hour growth of virulent typhoid bacilli on gelatin plates was washed down with four or five cubic centimeters of sterile distilled water, and heated at 60° centigrade. The suspension was centrifuged, the supernatant fluid decanted, and the sedimented bacilli dried in vacuo. The dried residue was then ground with sodium chloride crystals, in an agate mortar, for two or three hours; sterile water was added, drop by drop, in the proportion of ten grams of water to each three grams of bacilli, and the resulting emulsion heated at 60° centigrade for two hours. After warming, the solid particles were allowed to settle for three days, heating occasionally for half an hour at 60° centigrade, after which the supernatant fluid was poured into ten volumes of absolute alcohol, and the white coagulum which formed was dried in vacuo. Ten milligrams of the pulverized precipitate was then dissolved in one cubic centimeter of distilled water, and one drop of this solution was used for each test. Chantemesse obtained positive reactions in all of the seventy cases of typhoid fever examined, and negative reactions in forty-nine of fifty control cases. The one control case which reacted was a tuberculous individual "who probably had the disease two years before." The typical reaction appeared within two or three hours as a reddening of the conjunctiva which rapidly spread to the caruncle, followed after a short interval by the appearance of lacrimation and a fibrinous exudate. He emphasized the fact that injection of the conjunctiva and of the caruncle was still evident twenty-four hours after it appeared, and occasionally persisted as long as six days; that the response was more marked in patients ill with typhoid fever and in convalescents from the disease, than it was in normal persons or in persons ill with other diseases; and that in no instance did dangerous local symptoms develop.

Several months after the publication of Chantemesse's article, Kraus, Lusenberger and Russ[2] observed that the method offered difficulties, since the efficacy of the test preparation is dependent on the toxicity of the bacilli, and that therefore the results of different observers are comparable

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only when a toxin of uniform determined strength is used. They made an elaborate series of observations with various extracts of typhoid, paratyphoid and colon bacilli, and with tuberculin, and found that all of these caused slight inflammatory changes in the conjunctivæ of healthy persons, of patients ill with typhoid fever or suffering from other diseases, and concluded that, inasmuch as the reaction is not specific, it is of no value.

The work of these observers, however, is subject to criticism, first, because they used test solutions prepared according to a different technic than that recommended by Chantemesse; second, because in making the test they used only one-tenth the amount recommended by him; and third, because they failed to regard the persistence of the reaction in interpreting their results.

In the following year, Prevel [3] published the results of the ophthalmo-reaction in five hundred cases of typhoid fever, "collected for the most part from the service of Chantemesse." He regarded the reaction of value because of its constant presence in typhoid fever, its absence in other febrile conditions, its remarkable agreement with the Widal reaction, and concluded that a reaction which "persists two days after the installation of the reagent into the conjunctival sac always signifies typhoid fever, though it may have occurred several years before."

Orszag [4] used "extracts of virulent typhoid bacilli obtained post mortem" and obtained positive reactions in all of the fifteen cases of typhoid fever tested, and also in seven of eighteen convalescents from the disease. In spite of these findings, he states that "the test is not practical as no constant toxin can be obtained," and that the reaction is positive in normal persons and in those ill with diseases other than typhoid fever.

Malisch [5] employed in his work a reagent prepared by Merck & Co., according to the technic of Chantemesse. The firm standardized the preparations made by them in terms of the minimal lethal dose for guinea-pigs weighing two hundred and fifty grams, and recommended the use of one-seventieth of a minimum lethal dose for each test. Malisch made observations on fifty-four cases of typhoid fever, in the febrile stage of the disease, and obtained positive reactions in all of them. Of sixty-six patients, afebrile or convalescent, 66 per cent showed positive reactions; of sixty patients, ill with diseases other than typhoid fever, 10 per cent reacted positively; and of fifty normal persons only three showed a "slight, very transitory conjunctival reddening." He found further, that of thirteen cases of typhoid fever seven gave a positive reaction when an extract of *Bacillus paratyphosus* was used as the antigen, and that of eleven typhoid fever patients, all showed the marked conjunctival inflammation when an extract of the colon bacillus was applied to the eye. He stated that, although the reaction is not absolutely specific the response in patients infected with the *Bacillus typhosus* is more constantly present, is more marked and persists for a longer time than it does in other conditions.

Meroni [6] used a different antigen. This author precipitated bouillon cultures of typhoid bacilli with absolute alcohol and dried the precipitate in vacuo. One gram of the pulverized residue was dissolved in 10 cubic centimeters of normal salt solution, and two drops of this solution were used in making each test. With this reagent Meroni obtained positive results in all of the eighteen typhoid fever patients examined, and negative results in eighteen patients ill with other diseases. Like Chantemesse, he too emphasizes as diagnostic the persistence of the reaction longer than six hours after its appearance.

Hamburger [7] modified the preparation of the reagent even more, employing the aqueous extract of an emulsion of typhoid bacilli containing three thousand million organisms in the cubic centimeter. He examined forty-eight cases with the following results: twenty-seven cases of typhoid fever all reacted positively, fifteen cases of other diseases all reacted negatively, and of six cases, clinically typhoid fever, but having negative blood cultures and agglutination reactions, four reacted positively. He stated that the intensity of the reaction bears no relation to the stage of the disease, except in so far as it is perhaps more intense during the febrile period.

Floyd and Barker [8] considered Hamburger's reagent "too strong," and used a similar preparation of one-third the strength, *i. e.*, aqueous extracts of a suspension containing one thousand million bacilli in a cubic centimeter. They obtained positive reactions in 96 per cent of ninety-three cases of typhoid fever and negative reactions in 84 per cent of twenty-four "controls." The four "controls" reacting positively were all tuberculous, and in all the injection of the conjunctiva disappeared in from three to five hours According to these authors, the reaction is elicited only during the active stage of the infection, from the third day to the seventh week; it disappears during convalescence and reappears in relapses. The intensity of the response is greatest during the second week of the disease and in very toxic cases. They could establish no parallel between the results of the ophthalmo-reaction and the agglutination phenomenon, whereas a close parallel between it and the result of the blood culture was apparent. In six cases, having a positive eye test and a negative Widal reaction, the *Bacillus typhosus* was later recovered from the blood.

About the same time that the last cited article appeared, Beckers [9] stated that the reagent of Chantemesse, when used as directed by that author, was "much too strong." He formed this conclusion from the fact that six normal men gave positive eye reactions when tested with it. Using a dilution of the antigen of one-tenth of the strength recommended by Chantemesse, however, Beckers obtained positive results in seven of eight cases of typhoid fever and negative results in all of "several" normal people.

The large number of cases of typhoid fever annually treated in the wards of the Johns Hopkins Hospital affords an excellent opportunity for the study of this disease, and, in June of this year (1910), an investigation of the merits of the ophthalmo-reaction as an aid in the diagnosis of it was undertaken.

In the first series of observations made, the test solution was prepared exactly as recommended by Chantemesse, and of five cases of typhoid fever tested only three showed a positive reaction. The failure of two undoubted cases of typhoid fever to react, together with the statement of several authors that the weakness of the test lay in the fact that no uniform antigen could be obtained, suggested the necessity of modifying the preparation of it. The modifications had in view the securing of a substance which would cause a reaction in all cases of typhoid fever and which would not cause a reaction in those ill with other diseases, or in healthy individuals.

To Secure an Antigen Which Would Cause a Reaction in all Cases of Typhoid Fever.

One of the first cases tested furnished an idea which was followed out in all of the subsequent work. The patient in his initial infection gave a negative eye reaction on the nineteenth day of the disease. One week later a well defined relapse developed, with exacerbation of fever, a palpable spleen and the presence of typhoid bacilli in the circulating blood; and now a drop of the test solution in the other eye caused a marked inflammatory reaction of the type which later will be described as specific.

The explanation suggested itself that perhaps the first instillation in the right eye had so sensitized the patient that he reacted to the second test. This possibility was excluded by the failure of similar repeated instillations in non-typhoids to cause a like response.

It next seemed plausible that the relapse might be the result of a reinfection of the patient with a different strain of bacilli, and that he, therefore, reacted differently, because of different antibodies formed. Naturally, this inference called to mind Durham's theory of relapse in fevers.

Durham,[10] it will be remembered, regards any given infection "not as the result of the action of a number of identical infecting individuals, but as the result of the action of the sum of a number of infecting agents, each of which is similar, but not identical in nature." In other words, an apparently simple infection with a given organism is a complex phenomenon brought about by a number of varieties and subvarieties of that organism, each of which is neither identical with nor equivalent to the other. If in an infection, the number of varieties is approximately equal, a "normal or isozymic" infection results; whereas, if one or more of the varieties preponderate greatly, an "abnormal or anosozymic infection" occurs.

Evidence that such varietal quantitative differences between various strains of typhoid bacilli exist, is found in the work of Pfeiffer,[11] who showed that the protective bodies which appear in the blood are not equivalent in different typhoid convalescents; that is, "different sera contain unequal proportions of the constituent units which together are designated as antibody. Again, in the bacteriolytic, or Pfeiffer test in guinea-pigs, it had been found that a certain quantity of an immune serum will give complete lysis when one strain of *Bacillus typhosus* is used as the antigen, and only partial lysis results when another strain of the bacillus is used. Also, in agglutination tests, Durham showed that the smallest amount of a serum necessary to agglutinate all the bacilli in an emulsion of one strain, did not, of necessity, cause a similar complete agglutination of another strain.

This hypothesis would explain the relapse of our patient as follows: the initial infection was an "anisozymic" one, the patient producing immune bodies in large amounts against the predominating strain A, and relatively small amounts of antibodies against the less numerous members of strain B. As a consequence, though the patient overwhelmed the strain A, his serum was unable to prevent the multiplication and action of strain B, and he therefore suffered a demonstrable reinfection or relapse. Presumptive evidence in favor of this explanation is given by the fact that the serum of two rabbits, the one immunized with strain A, the other with strain B, agglutinated the strain, inoculation with which had called forth its production, in greater dilution than it did the other.

It is fair to assume that, inasmuch as in an infection with typhoid bacilli variations in the degree of the bactericidal and the bacteriolytic immunity are found, that quantitative variations at least in the degree of sensitization with different strains of the organism might occur. If this were true, an individual sensitized with one race of bacilli would show a marked reaction when a strain of the organism identical with the infecting one was used as the antigen, and a less marked reaction, or even no demonstrable response, when a heterologous strain was employed. To prevent, if possible, such variations in reaction, numerous strains of typhoid bacilli were used in making the test preparations, in the belief that the union of many races of the organism would neutralize these quantitative differences and yield a product of greater value.

Preparation of the Antigen.

Ten or more flasks, each containing about half a litre of plain bouillon, were inoculated with eighty different strains of typhoid bacilli and incubated at 37.5° centigrade, for twenty hours. The cultures were then centrifugalized, and the sedimented bacteria washed free of broth. A homogeneous suspension of the washed organisms was made in sterile distilled water and after heating in a water bath for two hours at 60° centigrade, was dried in vacuo. When thoroughly desiccated the mass was ground in an agate mortar with a small amount of sodium chloride crystals for three hours. With constant grinding, sterile distilled water was added drop by drop, in the proportion of ten cubic centimeters of water to each gram of pulverized bacilli, and the resulting emulsion warmed for two hours at 60° centigrade. Heating for half an hour daily was repeated on three successive days, after which the supernatant fluid was slowly poured into ten volumes of absolute alcohol and the white flocculi which formed were dried in vacuo. The dried residue was finally ground to a powder, and one drop of the solution of ten milligrams of it in one cubic centimeter of water was used for each test.

The powder is stable when kept in tightly sealed dark containers, and remains active for months. Solutions of the reagent in water, however, deteriorate rapidly, and often are useless after three or four days.

It is desirable to use fresh preparations in carrying out the test.

Technic of Carrying Out the Test.

The conjunctivæ of the two eyes are carefully examined for signs of inflammation and, if none are found, the test is made as follows: If the right eye is used, the patient turns his head towards the left side. Purse the lower lid with the fingers, and with an eye dropper instil one drop of the antigen solution into the inferior conjunctival sac, so that it runs to the median canthus. It is necessary to prevent sudden closure of the lids before the drop has been well distributed over the conjunctiva, and to caution the patient not to rub the eye.

The time of the instillation is recorded, and the eye examined at short intervals, during the first twenty-four hours.

Description of the Reaction.

A. Typical or Diagnostic.—Description based on the observations made in seventy-five cases of typhoid fever.

Within one to five hours after a drop of the test solution has been introduced into the conjunctival sac, there is generally a moderate grade of injection of the blood vessels of the palpebral conjunctiva of the lower lid, reddening of the caruncle, lacrimation, usually not marked and often lacking, and a drop of yellow pus in the conjunctival sac. When the reaction is very marked, there may be suffusion of the bulbar conjunctiva generally limited to the inferior one-third or one-half of it. The reaction is usually maximal within six to ten hours, when, in addition to the changes noted, there may be reddening of the skin of the lids, slight edema of the lids, and slight chemosis. In almost every case the palpebral conjunctiva of the lower lid is now a bright purple in color and velvety in appearance.

After the tenth hour, the signs of acute inflammation very slowly subside, but congestion of the conjunctiva of the lower lid is still marked after twenty hours, often after forty hours, and occasionally as long as two hundred and forty hours.

Even when the inflammatory response is very great, and it is not so unusual to find it so, there is rarely any complaint of symptoms. In the entire series of cases reacting only one patient volunteered the statement that his "eye felt warm," and not a patient complained of pain or of photophobia. When questioned, most of the patients stated that, aside from "the sticking together of the lids" or "the watering of the eye," they had no discomfort whatever. In no instance did signs of deep-seated ocular inflammation develop.

In summary the essential characteristics of the typical reaction are:

a. Congestion of the blood vessels of the palpebral conjunctiva, usually maximal in from six to ten hours, when the membrane is deep purple in color.

b. The persistence of this congestion for at least twenty hours.

c. Lacrimation, purulent exudate and bulbar suffusion.

B. A Typical or Non-specific Reaction.—Not infrequently, normal persons, or those suffering from diseases other than typhoid fever, show signs of conjunctival inflammation following the introduction of the typhoid antigen into the conjunctival sac. The response in these cases differs from that seen in patients with typhoid fever, in the more constant presence and greater degree of injection of the visceral conjunctiva; in the larger amount of purulent secretion formed, and, in what is of greatest significance, the less constant development of a reaction in the palpebral conjunctiva and caruncle. Even when injection of the latter does develop, it is less intense and more transitory, fading rapidly in four to fourteen hours.

The fact that reactions of this type occur has led some observers to doubt the specificity of the ophthalmo-reaction in typhoid fever.

Results of the Application of the Ophthalmo-Reaction in Typhoid Fever.

From a study of Table I it will be seen that in seventy-five cases of typhoid fever the ophthalmo-test was positive in seventy-one and negative in four.

Of the nineteen cases examined during the first week of the disease, all but one reacted positively, and in that case repeated blood cultures and agglutination reactions were negative.

Of the twenty-five patients tested during the second week of the disease, every one gave a positive reaction. One of these cases showed a negative reaction on the eighth day and a positive reaction on the twelfth day.

Of the fifteen cases in the third week of the disease two failed to give the typical response. One of these cases had a negative blood culture and Widal reactions; the other had a positive Widal reaction on the same day that the eye test was tried.

Seven cases were examined during the fourth week of the disease and all reacted positively; and of four cases in the fifth week all developed the typical response except one, and that one had completely recovered.

Two patients in the sixth week and one in the eighth week showed positive reactions.

The earliest appearance of the reaction was on the third day of the disease, the latest on the fifty-seventh day.

Of fifteen patients, convalescent and afebrile, only three still gave the specific response.

In four patients with a relapse the reaction was positive early in the stage of reinfection.

Inflammation of the conjunctiva was noted as early as one hour after the application of the antigen, the average interval before it developed being two and a half hours.

The maximum changes were usually apparent by the sixth

TABLE I.

	Clinical Diagnosis.	Blood Culture.		Widal Reaction.			Ophthalmo-Reaction.								Symptoms.
		Result.	Day.	Result.	Day.	Result.	Day.	Appeared	Maximum	Duration hours.	Pus.	Lacrimation.	Chemosis.	Edema Lids.	
1	Typhoid Fever.	+	7	0	7; 14; 21	+	5	2	6½	48	+ +	+	0	+	"Eye feels warm."
2	do	+	9	0	9; 15	+	7	2	5½	37	+	0	0	0	0
3	do	+	9	0	9	+	6	2	6	51	+	+	0	0	0
4	do	+	8	0	5; 15	+	7	2	4	34	+	+	0	0	0
5	do	+	8	0	6	+	6	3	9	28	±	0	0	0	0
6	do	+	4	+	4; 20	+	3	4	8	26	±	0	0	0	0
7	do	+	6	0	6	0	6	..	..	..	0	0	0	0	0
8	do	+	9	0	8	+	6	2	5	80	+ +	+ +	+ +	+	Curious absence of symptoms with flagrant reaction.
9	do	0	6; 11	0	10; 15	+	5	1¾	7	60	+	0	0	0	0
10	do	+	10	0 +	10; 47	+	7	3	6	48	+	0	0	0	0
11	do	+	6	0 0	5; 12	+	7	4	6	40	+	+	0	+	0
12	do	+	9	0	9	+	6	5	9	56	+	0	0	0	0
13	do	+	8	0 +	6; 24	+	6	2½	9	52	±	0	0	0	0
14	no	+	6	0	6	+	4	3½	5½	96	+	+	0	+	0
15	do	0	6	0	6	+	6	1	6	30	+	+	0	+	0
16	do	+	6	0	6	+	5	2	6	44	+	0	0	0	0
17	do	0	2	0	2; 18	0	2	..	..	..	+	0	0	0	0
18	do	0	8	+	8	0 +	8; 12	6	10	27	+	0	0	0	0
19	do	+	10	0	16	+	8	1¾	8	58	0	0	0	0	0
20	do	+	10	0	10	+	8	4	10	50	0	0	0	0	0
21	do	+	9	0	10	+	8	3	6	34	+	0	0	0	0
22	do	+	12	+	12	+	8	2	6	36	+	0	0	0	0
23	do	+	8	0	8	+	8	1¾	5	40	+ +	+	0	+	0
24	do	+	9	0 +	8; 45	+	8	2	4	45	+	0	0	+ red	0
25	do	+	11	0	10	+	9	3	7	48	+	+	0	0	0
26	do	+	10	0	10	+	10	2	11	28	+	+	0	0	0
27	do	+	8	+	8	+	11	8	16	40	+	0	0	0	0
28	do	0	6	0	14	+	10	4	12	26	+	0	0	0	0
29	do	+	11	00+	11; 18; 50	+	11	2	4	43	+	0	0	0	0
30	do	+	3	00+	8; 39; 50	+	11	3	7	34	+ +	0	0	0	0
31	do	+	5	0 +	5; 34	+	13	2	6	48	+	0	0	+	0
32	do	+	5	0 0	5; 25	+	13	2	4	27	+	0	0	0	0
33	do	+	7	0 0	8; 30	+	13	2	4	30	+	0	0	0	0
34	do	+	2	0 0	2; 12	+	13	2	7	29	+	+	0	0	0
35	do	+	8	0	12	+	14	2	6	48	+	0	0	+	0
36	do	+	8	0 0	8; 14	+	14	2	4	28	+	0	0	0	0
37	do	—	..	0	13	+	12	..	..	30+	+	0	0	0	0
38	do	—	..	+	19	0	19	..	..	..	+	0	0	0	0
39	do	—	..	+	21	+	18	..	..	40+	+	0	0	0	0
40	Perforation.	0	15	0	15	+	15	1	2	35+	+	+	+	+	0
41	Typhoid Fever.	0	37	0000	10; 17; 24; 51	0	17	..	..	..	0	0	0	0	0
42	do	+	16	0 0	10; 21	+	15	4	6	34	+	0	0	0	0
43	Perforation.	+	17	0	19	+	16	4	7	40	+	0	0	0	0
44	Typhoid Fever.	+	19	0	19	+	16	4	8	29	+	0	0	0	Quotidian chills. Eye test positive 3 days before B.C.
45	do	+	20	+	20	+	16	2	7	240	+	+	+	0	0
46	do	0	16	+	17	+	16	4	6	50	+	+	0	0	"Eye smarts."
47	do	+	6	0	16	+	16	3	5	48	+	0	0	0	0
48	do	+	16	+	16	+	16	3	10	30	+	0	0	0	0
49	do	+	15	00+	11; 15; 43	+	19	1½	7	65	+	+	0	0	0
50	do	+	19	0	21	+	19	3	7	33	+	+	0	0	0
51	do	+	22	0	22	+	20	1	5	32	+	+	0	0	0
52	do	+	21	+	40	+	21	2	6½	58	+	0	0	0	0
53	do	+	9	0	40	+	24	2	6	45	+	+	0	0	0
54	do	+	11	0 +	11; 31	+	24	1	6	49	+	+	0	0	0
55	do	—	..	0	14; 24	+	24	..	..	36	+	+	0	0	0
56	do	+	27	0 +	27; 49	+	25	3	7	60	+	+	0	0	0
57	do	+	13	000	7; 23; 32	+	25	2	6	60	+	+	0	0	0
53	do	+	16	0 0	14; 30	+	27	2	6	45	+	0	0	0	0
59	do	+	10	0 0	12; 22	+	27	1	6	29	+	+	0	0	0
60	do	—	..	+	22	+	30	..	..	30+	+	0	0	0	0
61	do	—	..	0	30	+	36	..	..	30+	+	0	0	0	0
62	do	—	..	0	15	+	42	..	..	30+	+	0	0	0	0
63	do	—	..	+	18	+	31	..	..	30+	+	0	0	0	0
64	do	—	..	0	27	0	40	..	..	..	+	0	0	0	Up and about. Well.
65	do	+	36	+	36	+	36	1	6	42	+	+	0	0	0
66	do	—	..	+	30	+	47	..	..	30+	+	0	0	0	0
67	do	—	..	+	20	+	43	..	..	30+	+	+	0	0	0
68	do	—	..	+	16	+	57	..	..	30+	+	+	0	0	0
69	do	+	10	0	10	+	9	2	6	25	+	0	0	0	0
70	do	+	14	0	10	+	10	2	7	30	+	+	0	0	0
71	do	+	10	0	10	+	9	2	10	42	+	+	0	0	0
72	do	+	7	0	7	+	5	1	7	42	+	0	0	0	0
73	do	+	14	0 0	15; 30	+	13	3	4	58	+	+	0	0	0
74	do	+	8	0 0	9; 21	+	7	2	3	32	+	0	0	0	0
75	do	+	5	+	8	+	3	2	6	50	+	+	0	0	0

hour, occasionally as early as the second hour, and in one case they were delayed until the sixteenth hour.

The average duration of the palpebral injection was forty hours, the extremes being twenty-five and two hundred and forty hours.

The intensity of the reaction showed no constant variation with the severity of the infection or with the stage of the disease, except that it was more constantly present and more marked in the febrile, greatly intoxicated patients.

Especially worthy of note was the absence of symptoms, even when the inflammatory response was very intense; and the tendency of the most marked response to be localized in the palpebral conjunctiva of the lower lid and in the caruncle.

The results of the ophthalmo-reaction and of the blood cultures showed a striking similarity. In many instances the former was reported positive before the *Bacillus typhosus* was identified in cultures and in a greater number of cases the appearance of a positive eye test antedated by many days a positive agglutination reaction. Further, in three cases clinically typhoid fever the eye test was positive, whereas repeated blood cultures and Widal reactions gave negative results.

A closer scrutiny of the table shows, too, that the Widal reaction was positive as early as the ophthalmo-reaction in only twenty-three per cent of the cases.

Results of the Ophthalmo-Reaction in Other Diseases and in Health.

A total of one hundred and ninety persons, normal or ill with diseases other than typhoid fever, were examined for conjunctival sensitiveness to "typho-protein." Many (eighty-four) of them were febrile, and, in the case of several, a tentative diagnosis of typhoid fever was made at the time the test was given. In this latter group especially the value of the ophthalmo-reaction as a diagnostic aid was apparent as the few illustrative cases here detailed will show.

Case 28.—A woman with fever, torpor and lethargy, on examination was quite negative except that the spleen was enlarged. When first seen the clinical picture closely simulated typhoid fever and it was not until three days after the ophthalmo-reaction had been found negative, that the finding of the so-called "attenuated cocci of subacute infective endocarditis" in the blood made the diagnosis clear.

Case 43.—A man, on admission, had fever with a relative bradycardia, toxæmia with torpor, and a palpable spleen. The ophthalmo-reaction was reported negative within twenty-four hours after his entering the ward, whereas a negative report of the blood culture and Widal reaction was not available until twenty-four hours later. This patient soon developed arthritic lesions and a diagnosis of infectious arthritis was made.

Case 153.—A young boy with fever, bradycardia, leucopenia, and slight splenic enlargement. In this case, the diagnosis of typhoid fever seemed the more probable as the patient was one of a family of seven, six of whom were ill at the time with the disease. Here the finding of a negative ophthalmo-reaction was later supported by the negative results of blood culture and agglutination reactions, and by the short course of the disease with rapid defervescence.

Detailed analysis of more cases is unnecessary. Reference to Table II shows that in the examination of fifty-six pathological conditions in no instance was a reaction like that seen in typhoid fever noted. In many, several or all of the manifestations described above as characterizing the non-specific type of reaction did develop, *i. e.*, purulent secretion, lacrimation, injection of the bulbar conjunctiva, and transitory reddening of the palpebral conjunctiva and of the caruncle.

In two cases only did a reaction develop which was difficult to interpret. From both patients a history of previous infection with the *Bacillus typhosus* was elicited, and in both the injection of the palpebral conjunctiva of the caruncle was only of moderate grade and subsided in less than eighteen hours.

The striking dissimilarity between the conjunctival reaction following the instillation of the test solution into the conjunctival sac of persons having typhoid fever, and of those ill with other diseases or normal, must be apparent, and speaks strongly for the specificity of the reaction.

Nature of the Typhoid Ophthalmo-Reaction.

It is now a well known fact that when a foreign protein is introduced into the body, by a parenteral route, a condition of hypersensitiveness results, and that this condition of altered response to a second dose of the antigen is specific. The existence of such an allergic, anaphylactic or hypersensitive state may be manifested by a general reaction, so violent as to lead to an acute lethal exitus, or by local manifestations of varying degrees of severity.

Typhoid fever is the result of a general infection with the *Bacillus typhosus*. The clinical symptoms are due to the action on the organisms of specific antibodies (bacteriolysins) in the serum of the patient, leading to the liberation of endotoxins. The endotoxins are themselves of a protein nature or are bound in some intimate way with the proteins of the bacilli. Hence it seems logical to infer that a patient infected with the *Bacillus typhosus* will develop a condition of allergy or anaphylaxis to the proteins derived from this organism.

Complete proof of this hypothesis unfortunately cannot, as yet, be given. A general or constitutional reaction we may not attempt to produce in a patient already overwhelmed by his infection, and experimentally we can glean no data, for the reason that typhoid fever has not been successfully produced in animals. This much can be shown, however, that guinea-pigs can be so sensitized by intraperitoneal injections of typho-protein, that a second toxic dose, introduced intravenously or by the post-orbital route, will cause acute fatal anaphylactic shock.

Local manifestations of an allergic condition in man have usually been produced by applications of the antigen to the conjunctival or to the nasal mucosa, by inunction or by intradermal or subcutaneous injection. The ophthalmo-reaction in tuberculosis is perhaps the best known example of a local anaphylactic reaction, and a parallel between it and the ophthalmo-reaction in typhoid fever can readily be drawn.

Both diseases result from infection with a bacillus; in both the general symptoms proceed from the reaction of the tissues of the body to the toxic substances liberated from the infecting

TABLE II.

	Diagnosis.	Febrile.	Afebrile.	Ophthalmo reaction.	Remarks.
1	Cerebrospinal lues	..	+	Negative.	Purulent secretion. Visceral injection lasting 10 hours.
2	Pulmonary tuberculosis	..	+	....do....	Purulent secretion.
3	....do	+	..	....do....	Do.
4	....do	+	..	....do....	No signs of reaction.
5	....do	+	..	....do....	Do.
6	....do	..	0	....do....	Do.
7	....do	+	..	....do....	Do.
8	....do	..	0	....do....	Small amount of pus in sac. Slight injection bulbar conjunctiva.
9	....do	..	0	....do....	Small amount of pus in sac.
10	....do	+	..	....do....	Slight injection lower half bulbar conjunctiva.
11	....do	..	0	....do....	No signs of reaction.
12	....do	+	..	....do....	Do.
13	....do	+	..	....do....	Drop of pus at median canthus.
14	....do	+	..	....do....	Slight injection bulbar conjunctiva persisting 8 hours.
15	....do	+	.	....do....	Slight injection bulbar conjunctiva persisting 6 hours.
16	....do	..	0	....do....	Drop of pus at median canthus.
17	....do	..	0	....do....	Lids matted with dried secretion.
18	....do	+	..	....do....	Do.
19	....do	..	0	....do....	No signs of reaction.
20	....do	+	..	....do....	Caruncle reddened. Injection persisted 7 hours.
21	....do	..	..	....do....	No visible reaction.
22	....do	+	0	....do....	Much purulent secretion. Slight bulbar injection.
23	....do	..	0	....do....	No purulent secretion. Slight bulbar injection.
24	....do	+	..	....do....	No purulent secretion or bulbar injection.
25	....do	+	..	....do....	Do.
26	....do	+	..	....do....	Do.
27	....do	+	..	....do....	Do.
28	Subacute infectious endocarditis	+	..	....do....	Clinically suggested typhoid fever. Blood culture showed attenuated cocci.
29	....do	+	..	....do....	Clinically suggested typhoid fever. Blood culture showed attenuated cocci.
30	....do	+	..	....do....	Purulent secretion and bulbar suffusion.
31	Malarial fever, tertian	+	..	....do....	Do.
32	....do	+	..	....do....	No evident reaction.
33	....do	..	0	....do....	Do.
34	....do	+	..	....do....	Do.
35	Malarial fever, æstivo autumnal	+	..	....do....	No evident reaction, except pus at canthus.
36	....do	+	..	....do....	Slight bulbar injection lasting 4 hours.
37	....do	+	..	....do....	Slight bulbar injection lasting 6 hours, with pus in sac.
38	....do	+	..	....do....	No evident reaction.
39	Chronic lymphatic leukæmia	..	0	....do....	Do.
40	Catarrhal jaundice	+	..	....do....	Do.
41	....do	+	..	....do....	Do.
42	....do	+	..	....do....	Do.
43	Infectious arthritis	+	..	....do....	Injection of visceral conjunctiva.
44	....do	+	..	....do....	Do.
45	....do	..	0	....do....	Do.
46	Psychoneurosis	..	0	....do....	Do.
47	....do	..	0	....do....	Injection of visceral conjunctiva lasting 7 hours.
48	....do	..	0	....do....	Injection of visceral conjunctiva.
49	....do	.	0	....do....	Do.
50	....do	..	0	....do....	Do.
51	....do	..	0	....do....	Do.
52	....do	..	0	....do....	Do.
53	....do	..	0	....do....	Do,
54	....do	..	0	....do....	Do.
55	....do	..	0	....do....	Do.
56	Chorea	+	..	....do....	No visible reaction.
57	Chorea with endocarditis	+	..	....do....	Do.
58	Uncinariasis	+	..	....do....	Do.
59	Myocardial insufficiency	..	..	....do....	Do.
60	....do	..		....do....	Do.
61	....do	..	..	....do....	Do.
62	....do	..	..	....do....	Do.
63	....do	..	..	....do....	Do.
64	....do	..	..	....do....	Do.
65	Myocardial insufficiency. Broncho-pneumonia	+	..	....do....	Do.
66	....do	+	..	....do....	Do.
67	Myocardial insufficiency	..	0	....do....	Do.
68	Myocardial insufficiency. Jaundice	..	0	....do....	Do.
69	....do	..	0	....do....	Small amount of purulent secretion.
70	Myocardial insufficiency	..	0	....do....	No visible reaction.
71	....do	..	0	....do....	Injection lower third bulbar conjunctiva.
72	Myocardial insufficiency. Acute nephritis	..	0	....do....	No visible reaction.
73	Myocardial insufficiency. Pulmonary infarction	+	..	....do....	Do.
74	Myocardial insufficiency	+	..	....do....	Do.
75	....do	..	0	....do....	Do.
76	....do	..	0	....do....	Do.
77	Myocardial insufficiency. Cerebral embolism	..	0	....do....	Do.
78	Myocardial insufficiency	+	..	....do....	Injection lower third of bulbar conjunctiva.
79	....do	..	0	....do....	No visible reaction.
80	....do	..	0	....do....	Do.
81	....do	+	0	....do....	Do.
82	....do	+	..	....do....	Injection of caruncle persisting 3 hours.
83	Acute lobar pneumonia	..	0	....do....	Lacrimation and purulent secretion.
84	....do	+	..	....do....	Slight injection lower third of bulbar conjunctiva.
85	....do	+	..	....do....	Small amount of purulent secretion.
86	Ulcus ventriculi	+	..	....do....	No visible reaction.
87	....do	..	0	....do....	Do.
88	Carcinoma ventriculi	..	0	....do....	Do.
89	....do	..	0	....do....	Do.
90	....do	..	0	....do....	Do.
91	Gastric neurosis. Hyperacidity	..	0	....do....	Do.
92	....do	..	0	....do....	Do.
93	....do	..	0	....do....	No visible reaction.
94	....do	..	0	....do....	Do.
95	....do	..	0	....do....	Do.
96	Gastric neurosis. Anacidity	..	0	....do....	Do.
97	Epilepsy	..	0	....do....	Do.
98	....do	..	0	....do....	Do.
99	....do	..	0	....do....	Do.
100	Chronic constipation	..	0	....do....	Do.
101	....do	+	..	....do....	Do.

TABLE II—Continued.

	Diagnosis.	Febrile.	Afebrile.	Ophthalmo reaction.	Remarks.
102	Chronic constipation	..	0	Negative.	No visible reaction.
103	Acute gastroenteritis	+	..	do	Do.
104	Acute enterocolitis	+	..	do	Do.
105	do	+	..	do	Do.
106	Appendicitis	+	..	do	Reddening of caruncle persisting 2 hours.
107	do	+	..	do	No visible reaction.
108	Cholelithiasis	..	0	do	Do.
109	Cholelithiasis with jaundice	+	..	do	Do.
110	Acute cholecystitis	+	..	do	Do.
111	do	+	..	do	Lacrimation and small amount of purulent secretion.
112	Acute Peritonitis	+	..	do	No visible reaction.
113	Tuberculous peritonitis	+	..	do	Do.
114	do	+	..	do	Do.
115	do	+	..	do	Do.
116	Pleurisy with effusion	+	..	do	Do.
117	do	+	..	do	Do.
118	do	+	..	do	Do.
119	Miliary tuberculosis	+	..	do	Do.
120	do	+	..	do	Do.
121	do	+	..	do	Transitory injection of the bulbar conjunctiva.
122	Tertiary syphilis	..	0	do	No visible reaction.
123	do	+	..	do	Do.
124	Arterio-sclerosis	..	0	do	Do.
125	do	..	0	do	Do.
126	do	..	0	do	Do.
127	do	..	0	do	Much pus, lacrimation, bulbar injection and reddening of caruncle and palpebral conjunctiva lasting 12 hours.
128	do	..	0	do	No visible reaction.
129	Arterio-sclerosis. Broncho-pneumonia	+	..	do	Do.
130	Arterio-sclerosis	..	0	do	Do.
131	do	..	0	do	Do.
132	do	..	0	do	Do.
133	do	..	0	do	Do.
134	Cirrhosis hepatis	..	0	do	Do.
135	do	+	..	do	Do.
136	do	..	0	do	Do.
137	Aortic aneurism	..	0	do	Do.
138	do	..	0	do	Do.
139	do	..	0	do	Do.
140	Tabes dorsalis	..	..	do	Do.
141	do	..	..	do	Do.
142	do	..	..	do	Do.
143	General paresis	..	..	do	Do.
144	do	..	..	do	Do.
145	do	..	..	do	Do.
146	Acute anterior poliomyelitis	+	..	do	Do.
147	Epidemic cerebrospinal meningitis	+	..	do	Do.
148	Tuberculous meningitis	+	..	do	Do.
149	do	+	..	do	Do.
150	Acute mania	..	0	do	Do.
151	Acute cystitis	+	..	do	Do.
152	do	+	..	do	Do.
153	Acute pyelitis	+	..	do	Small amount of pus. Injection visceral conjunctiva.
154	Chronic nephritis	..	0	do	No visible reaction.
155	do	..	0	do	Do.
156	do	..	0	do	Do.
157	Chronic nephritis. Broncho-pneumonia	+	..	do	Do.
158	Chronic nephritis	..	0	do	Do.
159	Diabetes mellitus	..	0	do	Do.
160	Polyglandular dyscrasia	..	0	do	Do.
161	Pernicious anæmia	..	0	do	Do.
162	Acute bronchitis	+	..	do	Do.
163	do	+	..	do	Do.
164	do	+	..	do	Do.
165	Influenza	+	..	do	Do.
166	do	+	..	do	Lacrimation.
167	do	+	..	do	Bulbar suffusion.
168	Septicæmia-streptococcus	+	..	do	No visible reaction.
169	Septicæmia staphylococcus	+	.	do	Small amount of pus. Slight bulbar injection.
170	Spondylitis	..	0	do	No visible reaction.
171	Fractured spine	..	0	do	Do.
172	Cryptorchidism	..	0	do	Do.
173	Hodgkin's disease	..	0	do	Do.
174	Polyserositis	+	..	do	Do.
175	Morphinism	..	0	do	Do.
176	Amœbic dysentery	+	..	do	Do.
177	do	..	0	do	Do.
178	Normal adults	..	0	do	Do.
179	do	..	0	do	Do.
180	do	..	0	do	Do.
181	do	..	0	do	Do.
182	do	..	0	do	Do.
183	do	..	0	do	Do.
184	do	..	0	do	Do.
185	do	..	0	do	Do.
186	do	..	0	do	Do.
187	do	..	0	do	Do.
188	do	..	0	do	Drop of pus at median canthus.
189	do	..	0	do	Lacrimation.
190	do	..	0	do	Slight bulbar injection.

agent by the action of specific antibodies upon them. In both diseases the instillation of a weak solution of the specific antigen into the conjunctival sac causes the development of local inflammation. In neither disease does the conjunctival instillation of other antigens result in a similar tissue response, nor do normal individuals or those ill with other diseases show a like reaction, when similarly treated. In other words, the response is specific.

It is true that neither a conjunctival nor skin reaction has been produced in animals sensitized with typho-protein. It is equally true that similar failure has resulted when the production of local reactions has been attempted in animals similarly sensitized with tuberculo-protein.

Animals infected with typhoid bacilli show neither local nor general manifestations when typho-protein is injected subcutaneously, whereas in tuberculous animals both types of reaction have been successfully produced. But for this apparent difference a ready explanation is found in the fact that, whereas tuberculosis does occur spontaneously in animals and can be experimentally produced in them, the reverse is true of typhoid fever.

From the foregoing data, strong presumptive proof, at least, is given that the ophthalmo-reaction in typhoid fever is analogous to the ophthalmo-reaction in tuberculosis, and that if the latter is a manifestation of allergy, so in all probability is the former.

The specificity of the ophthalmo-reaction in typhoid fever is not negatived by the occurrence of atypical responses in healthy individuals. Such reactions may rather be interpreted as an indication of a "group anaphylaxis." Every one harbors in his intestinal tract myriads of colon bacilli which, like typhoid bacilli, belong to the so-called dysentery group. From time to time, possibly as the result of trauma of the mucosa or of infection with other organisms, these bacilli find a portal of entry, and as a consequence of the invasion of the tissues by them, the body reacts by the formation of antibodies against them. The bacteriolysins formed cause destruction of the bacilli, colon-protein is liberated, and sensitization probably develops.

Evidence for this assumption, that in health there is probably a certain degree of hypersensitiveness to the protein of colon bacilli, is found in the presence of colon agglutinins and bacteriolysins in the serum of healthy individuals. More direct proof is furnished by the observation that a solution containing one half to one milligram of colon-protein prepared in the same way as the typho-protein used in the ophthalmo-reaction, when applied to the conjunctiva caused an inflammatory response in nearly 75 per cent of the fifty normal persons examined. That sensitization with the protein of colon bacillus carries with it a certain degree of sensitization to the protein of typhoid bacilli, can be shown experimentally. In a series of preliminary experiments we have found that guinea-pigs sensitized by intraperitoneal injections of typho-protein can be fatally intoxicated by a post orbital injection of colon protein, and, similarly, that intraperitoneal injections of colon protein will render guinea-pigs hypersensitive to typho-protein.

Conclusions.

1. A solution of one-third to one-half of a milligram of "typho-protein" in a drop of water, when instilled into the conjunctival sac of a patient ill with typhoid fever, causes a typical inflammatory reaction.

2. The most constant results are obtained when the "protein" is derived from numerous different strains of the bacilli.

3. The typical response shows definite characteristics:

a. It is limited to or is maximal in the palpebral conjunctiva of the lower lid and in the caruncle.

b. It appears in one to five hours, reaches its maximum intensity in about six hours, and persists twenty-four hours or longer.

c. The most characteristic sign is the deep purple congestion of the palpebral conjunctiva of the lower lid and of the carunele.

4. The reaction is relatively specific and can be differentiated readily from the response produced in other diseases and in health.

5. The results of the typical ophthalmo-reaction are in close agreement with those of the blood culture, and in establishing a diagnosis early in the disease the eye test is apparently of greater assistance than is the Widal reaction.

6. A positive reaction is obtained most often during the active febrile stage of the disease and is least often shown by patients convalescent and afebrile.

7. The advantages of the test are its simplicity, the fact that it can be applied and interpreted by the physician, the rapidity with which it becomes manifest, and the absence of any discomfort to the patient.

8. The ophthalmo-reaction in typhoid fever is probably to be considered as an evidence of an allergic state, in spite of the fact that in typhoid fever an anaphylactic condition is not generally believed to exist.

9. The atypical reactions developing in healthy individuals may likewise be considered as evidence of a group sensitization to members of the so-called "Dysentary Group of Bacilli."

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THE STRAUSS TEST FOR HEPATIC INSUFFICIENCY.

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The purpose of this study was to determine by clinical application the value of the Strauss test for hepatic insufficiency[1]. The need for clearer information as to the condition of the liver than is given by present methods of physical examination was well illustrated by the recent occurrence in the Johns Hopkins Hospital of two cases of acute degenerative hepatitis, in neither of which was the diagnosis made. In both cases a very large part of the liver parenchyme had been thrown out of commission by the advanced destructive lesion present—a fact which a reliable test for hepatic function would have revealed.

Technique.

In making this study the following technique was employed. The night before the urinary examinations were to be made, all food was discontinued after the evening meal. At 6 a. m. the following morning, a specimen of urine was obtained and the patient given 100 gm. of levulose with 400 cc. of water or weak tea. Additional specimens of urine were collected at 7, 8, 9 and 10 a. m. The patient was then allowed to receive the diet which he had been getting before the test. The 5 specimens of urine (1 obtained before, and 4 after the levulose was ingested) were examined for levulose. The test of Seliwanoff was used for the detection of the levulose. Reliance, however, was not placed on this test alone; in cases about which there could be the slightest doubt, Borchardt's test was also made. In a few cases Fehling's and Nylander's tests were used; and when any doubt still persisted, Cipollina's modification of the phenyl-hydrazine test was regarded as the court of last appeal. Jolles' modification of the Ihl-Pechmann test and Hammarsten's spectroscopic test were made in a few cases.

The Reaction of Seliwanoff.—A few cubic centimeters of a mixture of equal parts of water and concentrated hydrochloric acid are heated for about 1½ minutes with an equal amount of urine and a few crystals of resorcin. If levulose is present, a reddish brown color appears, followed by a brownish precipitate which is soluble in alcohol[2]. A fair number of normal urines give a transient reddish color when heated with hydrochloric acid, but the color soon disappears and no sediment forms; when levulose is present, on the other hand, the test becomes more characteristic as the urine cools. Indican may give a reddish color similar to that given by levulose, though the precipitate, if well-marked, excludes indican. If doubt on this score exists, however, the indican should be removed by adding an equal quantity of Obermayer's reagent to a few cubic centimeters of urine, and extracting in a Strauss funnel with chloroform. The chloroform is then allowed to run off, and the Seliwanoff and Borchardt tests are made.

The Reaction of Borchardt.—This test should be made whenever the Seliwanoff reaction is not perfectly convincing. The urine is heated with hydrochloric acid and resorcin, as in the Seliwanoff test. It is allowed to cool and made alkaline in an evaporating dish with sodium carbonate. It is then poured into a test tube and shaken out with acetic ether, to which, if levulose is present, a yellow color is imparted.

Cipollina's Modification of the Phenyl-hydrazine Test.—Four cubic centimeters of urine, 5 drops of pure phenyl-hydrazine, and 0.5 cc. of glacial acetic acid are boiled, over a small flame, for 1 minute. Four or five drops of KOH solution (sp. gr. 1.16) are added, and the mixture again boiled gently for a few seconds. It is then allowed to cool and examined for crystals of phenyl levulosazone. If none form, filter, wash the filtrate through with 60 per cent alcohol, and evaporate over a water bath. Allow to cool and examine for crystals of phenyl levulosazone.

Precautions.

Certain precautions are necessary in performing the Strauss test. Levulose, in large amounts, is sometimes nauseating and the patients may vomit after taking it. Unless this fact is kept in mind the test may be regarded as negative when really no levulose has been ingested. The reaction of Seliwanoff, though in general satisfactory—particularly when a heavy brownish precipitate forms—must be controlled as already indicated. In the presence of much indican, great care must be used. The reaction is not extremely delicate and was negative in several of my cases in which crystals of phenylglucosazone could be readily obtained. The Seliwanoff and Borchardt tests usually agreed; in one or two cases they were at variance.

Material Studied.

A series of fifty-two cases was studied, the patients being taken pretty much at random from the medical and surgical wards of the Johns Hopkins Hospital. Of these 52 patients, a positive diagnosis of hepatic disease could be established clinically in 12. In 38 cases the liver was absolutely normal, the majority of these patients being admitted to the surgical service for some strictly surgical condition. In two cases the clinical picture was not clear, cirrhosis of the liver being suspected but not established.

[1] Strauss: Deutsche med. Wchnschr., 1901, XXVII, 757.

[2] Great confusion exists in the directions for the Seliwanoff test to be found in the literature. The technique is carelessly described; the amount of HCl to be added is variously stated, and the impression is always conveyed (even in Seliwanoff's original report [Ber. d. d. chem. Gesellsch., 1887, XX, 181]) that the typical color reaction appears promptly. As a matter of fact it is usually necessary to heat the specimen, by boiling in the flame for about one minute, or by leaving in boiling water in a water bath for several minutes, in order to get satisfactory results.

RESULTS.

The results obtained may be summarized as follows:

- I. Liver normal clinically: 38 cases
  - Alimentary levulosuria present, 9 cases (23.68%)
    - Marked reaction, 5 cases
    - Moderate reaction, 3 cases.
    - Slight reaction, 1 case.
  - Alimentary levulosuria absent, 29 cases (76.31%)
- II. Liver abnormal clinically: 12 cases.
  - Alimentary levulosuria present, 10 cases (83.33%)
    - Marked reaction, 4 cases.
    - Moderate reaction, 1 case.
    - Hepatic change secondary, 5 cases.
  - Alimentary levulosuria absent, 2 cases (16.66%)
- III. Clinical picture doubtful: 2 cases. Alimentary levulosuria present, 2 cases (100%).

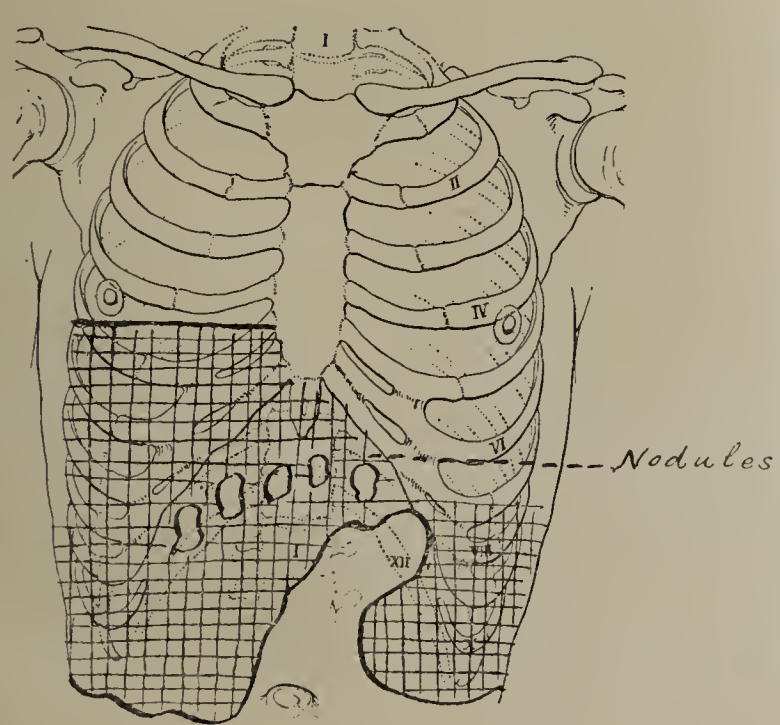
The general implications of these results are obvious at a glance. The preponderance of negative reactions in the normal cases and of positive reactions in the abnormal cases is, so far as it goes, evidence of the value of the Strauss test as indicative of the functional capacity of the liver. The presence, however, of a sufficiently large number of positive reactions in the normal group, and of two cases, in the abnormal group, with an absolutely negative reaction, is final proof that the test is not conclusive.

EVIDENCE AGAINST THE VALUE OF THE STRAUSS TEST.

Of the cases (29) with normal livers, which failed to show an alimentary levulosuria, nothing further need be said. The interesting and important cases are those (1) in which, with an abnormal liver, the reaction was negative, and (2) in which, with a normal liver, the reaction was positive. Of these cases a short account is given.

1. *Well marked signs and symptoms of advanced hepatic lesions, with total absence of alimentary levulosuria, i. e. negative Strauss test: 2 cases.*

1. T. F., male, 39 years old. Symptoms of 18 months' duration (enlargement of abdomen and recurring attacks of jaundice without pain). Diagnosis of syphilitic cirrhosis at first made, but Wassermann reaction was negative and there was no change in signs or symptoms under injections of salicylate of mercury. Marked ascites, some jaundice, and bile in the urine. Patient under observation for 9 months and no change in condition observed. Liver irregular and very hard; outlines as shown in chart:



Results of the Strauss test: *

AUGUST 26, 1911.

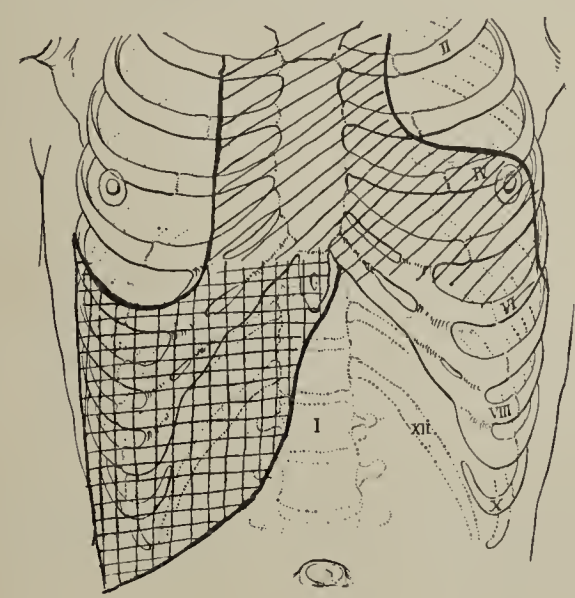
	S
1	0
2	0
3	0
4	0
5	0

AUGUST 27, 1911.

	S	B	F	N	PH
1	Specimens not obtained.				
2					
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0	0	0	0

2. H. F., male. Enlarged liver and ascites associated with myocardial insufficiency and arterio-sclerosis. Total absence of alimentary levulosuria.

Chart showing outlines of liver and cardiac dulness:



Results of Strauss test:

MAY 2, 1911.

	S	B
1	0	..
2	0	..
3	?	0
4	0	..
5	0	..

JUNE 7, 1911.

	S	B	I
1	0	..	..
2	0	..	..
3	?	0	0
4	0	..	..
5	0	..	..

The evidence afforded by these two cases, but particularly by the first, is of the greatest importance in estimating the value of the Strauss test. In Case 1 the anatomical changes in the liver were advanced and the symptoms were definitely due to the liver and to no other organ. Yet there was not a suspicion of lowered levulose tolerance, neither the Seliwanoff nor the more delicate tests indicating a trace of levulose in the urine. If it be argued that the Strauss test is one of function, not of anatomical condition, and that in these patients compensatory hypertrophy may have kept the functional capacity up to normal, the reply is that in that case it will be a difficult matter to accumulate evidence which will have any value at all in deciding the worth of the test as an aid in differential diagnosis, for compensatory hypertrophy could always be assumed to explain the negative results.

* In this and the succeeding tables:

S = Seliwanoff's test.
B = Borchardt's test.
F = Fehling's test.
N = Nylander's test.
PH = Phenyl-hydrazine test.
I = Indican test (Obermayer).
J = Jolles' test.

2. *Alimentary levulosuria, i. e. positive Strauss reaction, without signs or symptoms of hepatic disease: 9 cases.*

(a) Cases in which the *reaction was well marked: 5 cases.*

1. I. G., female. Fracture of fibula and os calcis. Liver not enlarged, reaching just to the costal margin; no symptoms indicating any hepatic lesions.

Results of the Strauss test:

	S	B	N	PH
1	0	..	..	..
2	+	+	+	..
3	+	+	+	+
4	+	?	+	+
5	0		..	..

2. R. M., male, weight 124 pounds. Tuberculous adenitis, cervical. Liver just palpable at the costal margin; no symptoms indicating any hepatic lesions.

Results of the Strauss test:

	S	B	I	F
1	0	..	?	0
2	0	..	..	..
3	++	+	+	+
4	+	+	..	+
5	+	+	..	+

3. H. D., male, weight 140 pounds. Fistula in ano; no enlargement of liver or symptoms indicating any hepatic lesions.

Results of Strauss test:

	S	B	N	PH
1	Specimen not saved.			
2	0	..	..	..
3	++	+	+	+
4	+	+	?	+
5	0	..	..	..

4. Male, weight 161 pounds. Tuberculous adenitis, cervical: no enlargement of liver or symptoms indicating any hepatic lesions.

Results of the Strauss test:

	S	B
6 a. m.*.....	0	..
9 a. m.....	++	+
10.30 a. m...	++	+
12.30 p. m....	+	+

* Specimens could not be obtained at the routine hours.

5. J. C., male, weight 140 pounds. In perfect health, nothing to indicate any disease of the liver either at present or in the previous history.

Results of the Strauss test:

	S	B	I	F
1	1	..	..	..
2	?	?	..	0
3	+	+	+	..
4	+	+	+	..
5	0	..	..	..

(b) Cases in which the *reaction was moderate: 3 cases.*

1. R. D., male, weight 125 pounds. Fracture of both bones of forearm. No enlargement of liver or symptoms indicating any hepatic lesions.

Results of the Strauss test:

	S	B	N	PH
1	0	..	..	..
2	0	..	..	..
3	++	+	+	+
4	Trace	Trace	..	..
5	Specimen not saved.			

2. T. F., male. Arterio-sclerosis and chronic nephritis; liver not enlarged, no symptoms indicating any hepatic lesion.

Results of the Strauss test:

	S	B	F
1	0	..	..
2	0	..	..
3	++	+	?
4	+	?	..
5	0	..	..

3. T. D., male, weight 151 pounds. Simple hernia; no enlarge- not enlarged, no symptoms indicating any hepatic lesions.

Results of the Strauss test:

	S	B	I	F
1	0	..	+	0
2	0	..	+	0
3	++	+	+	+
4	Trace	..	+	0
5	0	..	0	0

(c) Cases in which the *reaction was definite but slight: 1 case.*

1. R. G., female, weight 101 pounds. Paralysis of leg following an old anterior poliomyelitis. No enlargement of liver or symptoms indicating any hepatic lesions.

Results of the Strauss test:

	S	B	I	F
1	0	..	..	..
2	Specimen not saved.			
3	+	..	Trace	+
4	0	..	..	0
5	0	..	..	..

Summary: Liver normal, but reaction positive: 9 cases.

Marked reaction: 5 cases
Moderate reaction: 3 cases } 9 cases.
Slight reaction: 1 case

The Strauss reaction is thus seen to be positive in a certain number of cases with perfectly normal livers. Even if the most favorable light be thrown on the test by eliminating the moderate and slight reactions, 5 cases (13.15 per cent of the normal cases) remain, which show a strong reaction. The most marked reaction in the whole series was shown by a man weighing 161 pounds, who was in the hospital for tuberculous adenitis and whose liver was perfectly normal clinically. The urine in this case showed abundance of levulose four hours and a half after it was ingested and the test was still quite positive at the end of six hours and a half. None of the cases of hepatic disease gave a more marked test than this patient.

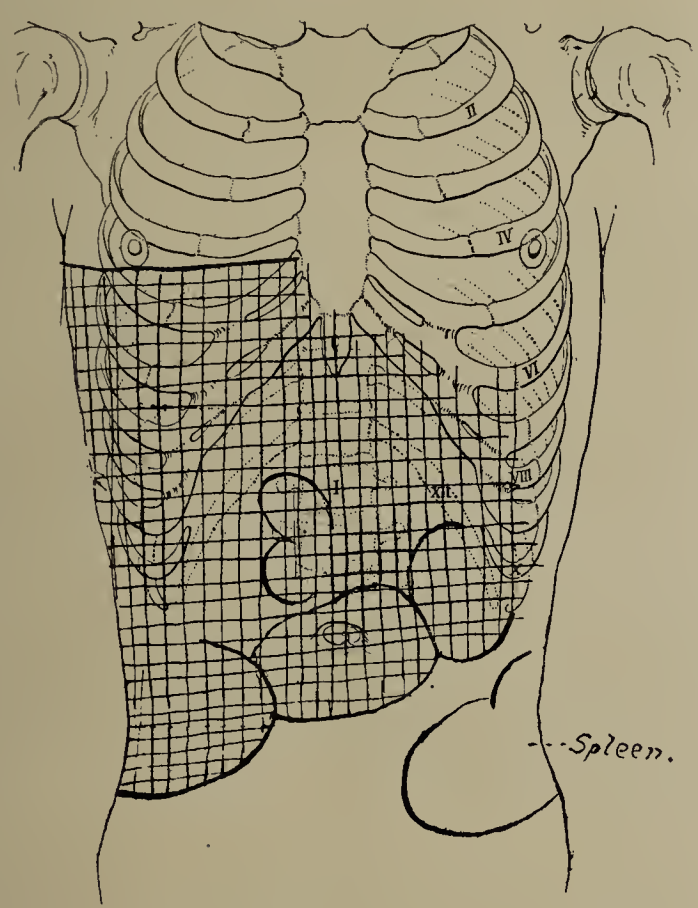
EVIDENCE FOR THE VALUE OF THE STRAUSS TEST.

So much for the evidence afforded by this study against the value of the Strauss test. There were, on the other hand, ten cases in the series in which definite hepatic lesions were accompanied by an alimentary levulosuria. In five of these the liver lesion was the primary and predominating feature of the clinical picture: in the remaining five there were symptoms indicating liver changes, but these were probably secondary to lesions in the heart and elsewhere.

3. *Definite clinical evidence of disease of the liver, accompanied by an alimentary levulosuria (i. e. positive Strauss test): 10 cases (liver lesion primary, 5 cases; liver lesion possibly secondary, 5 cases).*

(a) Cases in which the *reaction was marked: 4 cases.*

1. L. O., female, 34 years old. Has had three miscarriages, but no definite history of syphilis; Wassermann reaction negative; emaciation, anemia, enlarged spleen; liver irregular, hard and much enlarged (outlines as shown in chart).



Results of the Strauss test:

MAY 7, 1911.

	S	B	F	J
1	0	..	..	..
2	Trace	..	..	..
3	++	+	+	+
4	++	+	..	..
5	Trace	+	..	+

MAY 12, 1911.*

	S	I
1	0	..
2	0	..
3	0	† Free iodine.
4	++	† Free iodine.
5	0	..

* Test repeated, only 50 gm. of levulose being given.
† Patient is taking iodides.

2. N. F., male. Definite signs of cirrhosis of the liver with increase in the size of the organ (hepatic dulness reached from the IVth rib to a point 3 cm. below the costal margin in the right mammillary line). Large amount of fluid in abdomen; patient under observation for ascites for over 4 years, during which time he was tapped 27 times.

Results of the Strauss test:

	S	B	PH
1	0	..	..
2	0	..	..
3	+	+	+
4	+	+	+
5	Specimen not obt'n'd.		

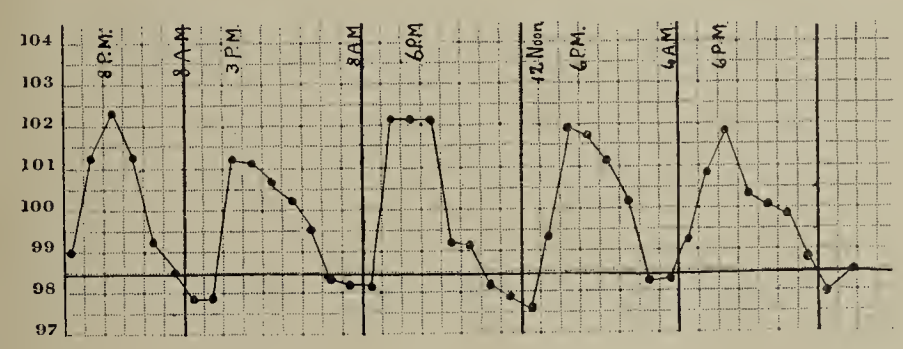
3. A. E., male, 57 years old. Had been suffering from dropsy, emaciation, and weakness for one year. Mitral and tricuspid insufficiency, right hydrothorax, edema of the extremities, fluid in the abdomen (10 liters withdrawn by tapping), enlarged abdominal veins; liver diminished in size, reaching from the IVth rib to a point 3 cm. above the costal margin in the right mammillary line.

Results of the Strauss test:

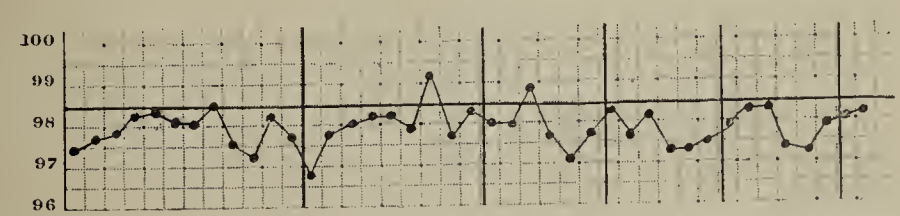
	S	B	I	F
1	Specimen not saved.			
2	+	..	..	+
3	++	Trace	Free iodine.*	+
4	+	?	+	..
5	?	0	..	0

* Patient is taking iodides.

4. A. B., male. This was a very interesting and important case under the care of Dr. Downey at the Baltimore Eye, Ear and Throat Hospital. The clinical features, while somewhat obscure, seem to justify its inclusion under the cases in which the liver was known to be diseased. The patient came to the hospital for an ulcerative lesion of the skin of the cheek, which was spreading into the ear. An attempt was made, by a plastic operation, to reconstruct the external auditory canal; at the same time a mild, chronic infection of the middle ear was treated by curettage, by way of the mastoid. Nineteen days after operation, the patient began to have fever, the character of which is shown in the chart. Daily chills occurred at the time of the maximal temperature.



There was nothing in the wound to account for this temperature; the leucocyte count was normal, and there was no relative increase in the polymorphonuclear neutrophiles. A septic process was excluded by the blood picture and by the total absence of symptoms. No malarial parasites could be found and the administration of quinine was quite without effect. There were sugges-



tive scars on the shoulders and legs and the Wassermann reaction was found to be strongly positive. A probable diagnosis of visceral lues was made, the case resembling those reported by Man-

naberg and others. The liver was very slightly enlarged, on percussion; palpation was of no help on account of abdominal rigidity. Specific treatment was instituted, beginning with salvarsan. The temperature promptly dropped to normal (see chart) and has remained so ever since (nearly three months later). The Strauss test, made before treatment was started, showed a very marked alimentary levulosuria; the Seliwanoff reaction, 5 hours after ingestion, was stronger than in any other case in the series, and remained strongly positive 6 hours after ingestion.

Results of the Strauss test:

JULY 1, 1911.

	S	B	PH
1	0	..	..
2	0	..	..
3	++	..	..
4	++	..	+
5	+++	..	..
6	+	..	+

After the patient had been on treatment for a little over two months and had been running a normal temperature for this length of time, the Strauss test was repeated. The Seliwanoff reaction was negative in all the specimens, as was the Fehling reaction; and, though sugar was shown to be present in the 2d, 3d and 4th specimens, by the Nylander and phenyl-hydrazine tests, the very marked difference from the reaction of two months previously was most striking.

Results of the Strauss test:

SEPTEMBER 21, 1911.

	S	B	F	N	PH
1	?	..	0	0	0
2	0	Trace	0	+	+
3	0	"	0	+	+
4	0	"	?*	+	+
5	0	"	0	?	0

* No true reduction; greenish precipitate on standing.

Visceral lues was probably present in this case. Conclusive evidence that the liver was involved is wanting; but the clinical similarity of the case to the reported cases of hepatic lues suggests this possibility. The complete cure by specific treatment and the simultaneous disappearance of a positive alimentary levulosuria are the interesting features.

(b) Cases in which the *reaction was moderate: 1 case.*

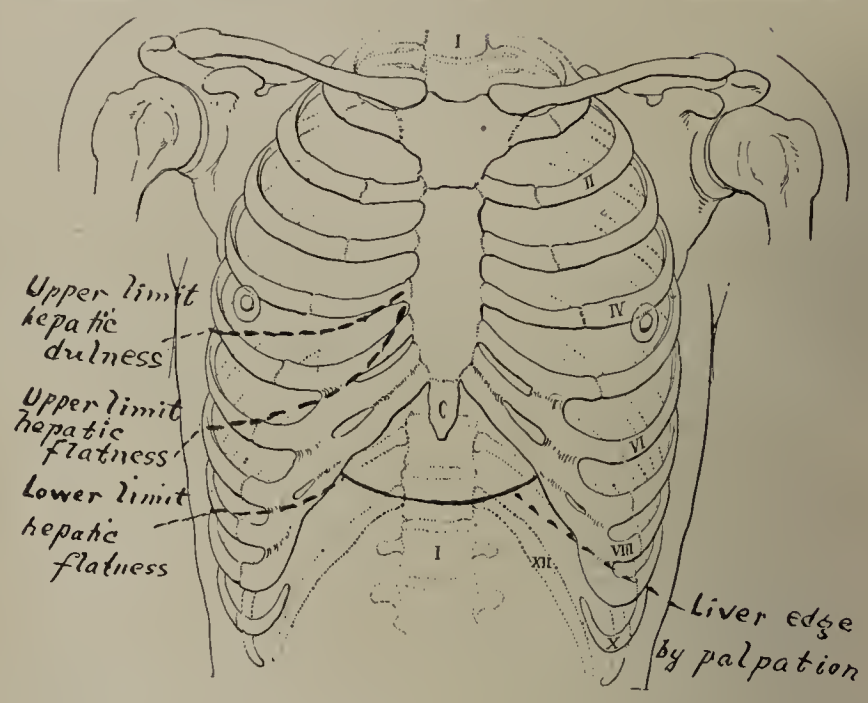
1. M. O., female. Jaundice, loss of weight, abdominal ascites, clay-colored stools, bile in the urine, no pain; nodular enlargement of the liver, the lower edge of which reached 7 cm. below the costal margin in the right mammillary line. Diagnosis of syphilitic cirrhosis.

Results of the Strauss test:

	S	B	N	PH
1	0	..	..	..
2	0	..	..	..
3	+	+	..	+
4	+	..	..	..
5	?	..	..	..

(c) Cases in which the *hepatic lesion was probably secondary: 5 cases.*

1. B. F., male. Edema of the legs, abdominal ascites, distention of the abdominal veins, hydrothorax; uncertain whether this was a case of cirrhosis of the liver or of polyserositis due to some other cause. Liver not enlarged, outlines as shown in chart:



Result of the Strauss test:

	S	B	PH
1	0	..	..
2	0	..	..
3	Trace	..	..
4	"	Trace	+
5	"	..	..

2. M. F., male. Myocardial insufficiency, lipomatosis, liver very slightly enlarged but causing no symptoms definitely referable to it.

Result of the Strauss test:

	S	B	I
1	0	..	..
2	0	..	..
3	+	+	0
4	0	..	..
5	0	..	..

3. W. M., male. Mitral insufficiency, edema of extremities, abdominal ascites, very slight jaundice, no enlargement of liver; doubtful whether the case is to be regarded as one of cirrhosis of the liver or myocardial insufficiency with chronic passive congestion.

Results of the Strauss test:

	S
1	0
2	Trace.
3	++
4	++
5	++

4. S. F., male. An obscure case; probably ulcerative aortic endocarditis and mitral insufficiency; enlargement of the liver which reached 4 cm. below the costal margin in the right mammillary line. Not primarily a liver case, though the hepatic changes undoubtedly played a part in the clinical picture.

Results of the Strauss test:

MAY 12, 1911.

	S
1	0
2	0
3	0
4	Trace.
5	0

JUNE 7, 1911.

	S	B
1	0	..
2	0	..
3	++	+
4	+	+
5	Trace	0

5. L. F., male. Jaundice, bilateral hydrothorax, abdominal ascites, edema of the legs, liver not enlarged.

Results of the Strauss test: *

	S	B
1	0	..
2	0	..
3	Trace	Trace
4	"	..
5	0	..

Summary: Liver abnormal and reaction positive: 10 cases.

Marked reaction: 4 cases
Moderate reaction: 1 case
Hepatic change secondary: 5 cases
} 10 cases.

Doubtful Cases.

In two cases of the series the clinical picture was suggestive of hepatic disease, but the diagnosis was uncertain. In both, alimentary levulosuria was present.

1. N. C., male. Gastric hyperacidity, liver slightly enlarged, reaching 1 finger-breadth below the costal margin. In the right mammillary line, edge palpable; no symptoms referable to the liver.

Results of the Strauss test:

	S	B	PH
1	0	0	0
2	Specimen not obt'n'd.		
3	++	+	+
4	?	?	+
5	0	..	..

2. H. C., male. Slight jaundice of the scleræ. Liver not palpated, no ascites; diagnosis obscure, possibly cirrhosis.

Results of the Strauss test:

	S	B	PH
1	0	0	0
2	0	..	..
3	+	+	+
4	+	+	..
5	+	+	..

Hypophyseal Cases.

Through the kindness of Dr. Cushing I had the opportunity to study a few hypophyseal cases with regard to the occurrence of alimentary levulosuria (16 examinations in 9 patients). The findings in this condition have already been published by Cushing;[3] and I mention the cases here simply by way of calling attention, in this connection, to the fact that at least one condition is known in which the levulose tolerance is upset by a lesion outside the liver. This disturbance in levulose tolerance may, of course, be brought about indirectly by some effect of the hypophyseal lesion on the liver function; but the fact that the disturbance occurs must be borne in mind in deciding as to the value of the Strauss test as an indication of disease of the liver.

Conclusions.

Alimentary levulosuria, as measured by the Strauss test, though not a constant feature, is present in a large proportion of cases of hepatic disease (83.33 per cent in this series). It is also present in a goodly percentage of normal patients (23.68 per cent in this series), and is absent in certain cases of definite and extensive disease of the liver. Neither its presence, therefore, nor its absence is to be regarded as conclusive evidence of the condition of the liver. The explanation which Strauss offers for the absence of alimentary levulosuria in certain cases of known liver disease, based on the assumption that hypertrophy has compensated for the loss of liver substance and has kept the levulose tolerance from falling below normal, may be correct; but it can hardly be advanced in support of the clinical value of the test as an aid in differential diagnosis. The test is one, it is true, of functional capacity and not of anatomical condition; but to assume a normal function in a definitely diseased liver, simply because there is no reduction of the tolerance for levulose, is to beg the question entirely. Similarly, to explain the positive reactions in normal individuals by assuming liver changes which have caused neither signs nor symptoms, is to settle the question quite independently of the only evidence available.

The reduction of the sugar tolerance and the presence of an alimentary levulosuria in patients with a functional hyperplasia of the posterior lobe of the hypophysis, indicates that the metabolism of levulose may not be quite the simple matter proposed by Strauss on the basis of certain suggestive results in hepectomized frogs.

To grade the amount of levulose, which normal patients should tolerate, according to the size of the liver (as indicated by the body weight) would be an improvement on the present method of using a constant amount of levulose for all patients, irrespective of size. For an adult weighing 70 kilos, the ingestion of 100 gm. of levulose without its appearance in the urine might be regarded as indicating a normal levulose tolerance. For heavier individuals proportionately larger amounts should be used. Unfortunately, large quantities of levulose are nauseating and cannot always be retained; so that this modified technique might be difficult to apply to very heavy patients.

The urinary examinations were made in the clinical laboratory of the Johns Hopkins Hospital, to which I had access through the kindness of Dr. Roger S. Morris.

* Patient was unable to retain the levulose, vomiting shortly after it was taken; so that the slight reaction, after the absorption of probably only a fraction of the levulose given, is more significant than it would otherwise be.

[3] Goetsch, Cushing and Jacobson: Johns Hopkins Hosp. Bull. 1911, XXII, 165.

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OBSERVATIONS ON SEPSIS AND ANTISEPSIS IN MEDICINE.[1]

By William Sydney Thayer, M. D.,
Professor of Clinical Medicine, The Johns Hopkins University.

In answer to the cordial invitation to speak before you this evening, I am going to ask your indulgence for a few reflections upon two phases of antisepsis in internal medicine.

The thoughts that I am going to try to bring before you to-night, though by no means original, have, however, haunted me more and more during the last several years and seem worthy of expression.

To one who is familiar with the history of medicine for the last fifty years, the transformation of surgery is a never ending source of satisfaction and of wonder. From the fundamental ideas of Lister, the evolution of our modern knowledge of the nature and causes of wound infection and of the measures necessary to prevent it, has progressed rapidly until the art of surgery has reached the remarkable position which it occupies to-day.

Twenty-five years ago, when I was a student, a surgical operation which involved the opening of a large joint or a serous cavity, was looked upon almost in the nature of an experiment. The critical "third day" was anxiously awaited. If that period were passed without fever, we drew a deep breath and felt that the main danger was over. How changed is all this to-day!

Time and again, twenty-five years ago, I have heard one of the most eminent of American surgeons say, in discussing some operative procedure: "If one be not careful, the first thing he knows he will find himself in the peritoneal cavity—*fatal peritonitis!*" Now that surgeon is opening the peritoneal cavity every day of his life with perfect assurance and with almost absolute safety. The dangers of infection are hardly considered. 'Tis only the question of the loss of blood, the condition of the heart and lungs and the effects of the long anaesthetization—and operations, of the possibility of which one barely dreamed, are performed with perfect security every day. With these facts we are all familiar. There is however one phase in the development of modern surgery which has not received the attention that it would seem to deserve, and that is the change in the character of the surgeon himself. One used to think of the surgeon of the past as a courageous, manly fellow with a good knowledge of anatomy, a steady and clever hand, skilful in the setting of the limbs and the application of bandages—a technician—not especially a student.

In many countries the surgeon used to be looked upon as belonging to a class somewhat lower than that of the physician—one who used his hands rather than his head. Not long ago it was the physician who was the more careful student, who was rather more likely to attend to minutiae in the practice of his art. The surgeon was the strong, vigorous, highly trained technician who, when the physician said "go ahead," was not afraid to bear the immediate responsibility of what was often an hazardous undertaking.

This relation does not, certainly, exist to-day. With the initiative of Lister, the surgeon has applied carefully, and conscientiously, the teachings of the laboratory to the practice of his art. He soon learned that the antiseptics which were destructive to the infectious agent were likewise injurious to the human organism; that the important question was not the application of antiseptics to the wound, but the prevention of the entrance of the infectious agent; not the treatment of the infection after it was present, but the prophylaxis against infection.

Hand in hand with this knowledge, a great change came over the practice of surgery and over the surgeon. From the dashing operator of a generation or two ago, the surgeon has become a man highly trained in the most careful and minute laboratory methods of prophylaxis. Every step in his extensive preparations for an operation must be carried out with exactness. These methods, many of which he and his associates have elaborated themselves by study in the bacteriological laboratory, are absolutely necessary for the success and safety of the operation. If he neglects one point in his precautions, the fatal infection may occur, and if it do occur, he feels that it must be his fault. Moreover, the public knows this, and the public, and, in some instances, the law, may hold him responsible. The average surgeon has become a very different man from his ancestor of fifty years ago. He is not only an exact and careful artist, but, far more than this, these habits and methods of work have led him into fields of research as a technician and as an investigator of which his forebears had little idea. Wherever the best surgery is done, other studies, not only in technique of the surgical art, but the pathology and etiology of disease are almost always pursued, and the leading surgeon of to-day is commonly an eminent physiological and pathological investigator.

Let us enter, for a moment, a modern surgical operating room:

In the ante-room, the sterilizers and autoclaves for the preparation of all material and instruments to be used in connection with the work—the surgeon himself going through a long, deliberate and exact process in the mere cleaning of his hands; donning his rubber gloves; his freshly sterilized coat; the cap upon his head; the sterile gauze about his nose and mouth; the operating room and table, both of material such as can most easily be kept clean and aseptic. The patient is placed upon the table—the region about the point of operation thoroughly cleansed and sterilized and covered with sterile gauze and towels. The nurse and the assistants, all prepared with like care in their sterile garments; the on-lookers, obliged to keep at a proper distance themselves, but even they, wearing

[1] Address delivered before the Jefferson County Medical Society, March 30, 1911, and reprinted, with permission of the editor, Dr. A. T. McCormack, from the Kentucky Medical Journal, August 15, 1911.

clean linen coats, those few who are to stand close to the surgeon, clad as he, in a sterile gown, but perhaps without armholes, so that even the temptation to touch is frustrated; their mouths and noses covered with sterile gauze, caps upon their heads: the absolute, scrupulous cleanliness of everything. Then note the freedom and safety with which the surgeon explores the most vital parts!

About the surgical operation of to-day there is a truly scientific exactness. Indeed, I am often moved to the reflection that we rarely feel the anxiety about *any* operation to-day that we used to feel about *every* operation when I was a house physician twenty-three years ago. All these preparations, all this experience, all these exact prophylactic methods are directed to save the life of the single individual patient on whom the surgeon is about to operate.

We look at the great achievements of surgery with unusual satisfaction and pride. We are fascinated and bedazzled by their magnitude. But when the layman asks us internists what we can show him in our branch of the medical art which can compare with the progress of antiseptic surgery we, on our own side, are not slow in pointing to the immense progress which has been made in our knowledge of the nature and causes of infectious diseases; of what we have learned as to many of the internal secretions, and as to their relations to various forms of disease; of the application of his knowledge to the treatment of diphtheria, of cerebro-spinal meningitis, of tetanus, of myxoedema and cretinism; to the prophylaxis of cholera and plague.

Is there anything more wonderful in surgery than our achievements in the prophylaxis against yellow fever? This progress is indeed wonderful and hopeful. Like the surgeon, we internists are giving ourselves to the careful study in laboratory and clinic of many pathological and etiological problems. But is there not perhaps another phase of the situation which we sometimes forget? The surgeon has banished hospital gangrene and wound infection from his wards by his own individual, careful, exact, prophylactic methods. Have we internists introduced like methods for the prevention of disease into our daily practice?

Let us go back to the operating room: While the surgeon, surrounded by his corps of assistants and nurses, is carefully at work, his medical colleague enters with his staff. Among them he passes into the room to take a glimpse at the work of his associate. He knows that the rules for the ordinary onlooker are not for him. He has not time for such excess of precaution; neither have his assistants. Making his way to the elbow of the operator while the assistants stand aside with their hands raised in the air, in order to avoid touching him, and forgetting that he has no gauze over his mouth, he talks freely with his face near the wound or over the tray in which lie the sterilized instruments. Then he leaves the room on his way to his special precincts, the wards.

It is summer time, the sun is shining through the open and unnetted windows. In the long line of beds lie the patients prepared for the visit. The polished floor, the white coverlets, the nurses in their trim white dresses and caps, the plants and flowers, lend an air of freshness and brightness to the room, which is cheering and enlivening.

The first patient is suffering from cardiac disease. Soon, however, we come to the bed of an individual with pulmonary tuberculosis. He should not be in the ward. Cases of pulmonary tuberculosis are not admitted to the wards of this hospital which is intended to care only for acute and curable diseases—but somehow or other this case has slipped in, and here he is. On the table nearby is his sputa cup—on its edge, a little of recently expelled sputa lies exposed, and on this bit of sputa is clustered a group of flies.

A short distance away, sitting up in bed and smiling, is a convalescent from typhoid fever with his thin chicken-like hair and that delicate complexion which suggests the scrubbing of frequent baths. A little farther on lies his neighbor, at the height of the disease, dull, apathetic, somnolent, with his eyes and mouth half open. About his lips and teeth are crawling flies that have come from whence—we know not, and are going—heaven knows whither. The doctor sits on the edge of the bed while making a physical examination. In the course of this examination, his hand, introduced under the bed clothes, detects the fact that the vesical sphincter has involuntarily relaxed. The doctor has a cold in his head, and interrupts his examination frequently by blowing his nose, his handkerchief in the hand which a moment ago was under the bed clothes. On leaving this patient he may, or may not, remember to wash his hands before passing on to the bed of a convalescent from influenza, who, interested in the progress of the visit, has put down his half-finished glass of milk, about which flies are already gathering.

The nurses, clean and bright in aspect, are called quickly from bed to bed—from the typhoid patient to the comsumptive, to the convalescent from influenza; when they can, they wash their hands, but it is often impossible.

On the wall of the ward is posted a notice setting forth the precautions which should be taken with regard to bed clothes, eating utensils, excreta and bath water of the patient with typhoid fever. As we pass out of the ward we look into the lavatory—how many of the precautions set forth in the directions upon the wall are here carried out? Sometimes, especially in a female ward, where the work is wholly under the charge of nurses, they may be observed strictly—too often, however, we find that the bed clothes of the typhoid and tuberculous patient are put into the common receptacle, and handled by more than one individual before they are sterilized. The directions for the disinfection of the stools and urine, of bed pans and urinals are carried out, alas, neither according to the letter, nor the spirit of the directions. The orderly, untrained and unimpressed with the importance of his work, moves from patient to patient without washing his hands, and carries out the printed precautions in a most perfunctory manner. The bath water, rarely sterilized, is allowed to run into the drain.

At the end of the visit, the physician washes his hands without removing his coat, and passes from the wards to his motor.

Next, perhaps, he visits a case of dysentery in a private family. Here again, the house is unnetted, the flies are omni-

present. Few or no precautions are taken with regard to the disposition of the excreta. A few directions may be given to the family with regard to the washing of their hands or to the sterilization of the excreta, but too often this advice is purely perfunctory, and is neglected by the family.

How rare it is to see really careful antiseptic precautions carried out in hospital or in private house! When we have seen these things, may we not well pause and reflect upon the difference between the procedure of the physician and that which we have seen in the operating room. What a contrast! On the one hand the cleanliness, the careful, rigid observance of most minute antiseptic and aseptic details, time-consuming though they be; on the other, lack of any adequate antiseptic measures. Patients with contagious diseases lying side by side with others in conditions peculiarly susceptible to infection; flies everywhere, ready to spread the contagion from individual to individual or from one patient to the nutriment of another; —physician, nurse and orderly circulating freely among all these patients—the physician in his ordinary clothes, sitting perhaps on the bed of a typhoid or dysenteric patient, using his handkerchief which he carries from place to place with him in his dirty hands; chaos and lack of system in the lavatory! Verily the contrast is striking! There may be, there are, exceptions to this picture, but too often it is true, and 'tis hardly to our credit as physicians.

"But," we object, stirred by this odious comparison, "the problem is different. You are comparing a ward with an operating room. Look at the surgical ward—are the conditions there essentially different?" Yes, they are different. There is, perhaps, much to desire in the surgical ward. The windows may be unnetted, the flies may be there, the conditions in the adjoining lavatory may not be essentially better than in the medical ward, but the typhoid, the tuberculous, the dysenteric patients, where are they? There is no one in the surgical ward with a contagious disease and those parts which might especially be subject to contagion are protected by elaborate bandages and dressings.

"Ah, yes," says the objector, "this is all very well, you know, however, what I mean. I am talking about individuals. Does not the medical man do his duty by the individual just as well as does his colleague, the surgeon? In the care of his patient with typhoid fever does he not give the same attention to minutiae? Is he not just as particular and just as conscientious? Is he any more open to criticism?"

Well, let us see. Where are the dangers of infection in the surgical wards? "In wounds," you answer. But these are protected in the most careful and scrupulous manner. "In the medical ward the patient with typhoid fever is already infected," you say, "and the problem is different." Very true, but when he is convalescent, is it not reasonable to believe that he is more subject to infections of other sorts than another? Is he not then more or less comparable to an open wound, and if so, how about his tuberculous neighbor and the flies? Are we protecting him as the surgeon protects his wounds? Hardly!

"But," says the objector, "this comparison is unfair. You are praising the surgeon because of his attitude to the individual case, and blaming the physician because he is not taking like measures to protect all of the rest of the world." In this assertion there are elements of justice, for the problems before the physician and surgeon to-day are somewhat different in detail if not in principle.

The surgeon, for the most part, is dealing with the wound which, with study and care, he has learned to make cleanly, and to preserve from infection. His duty to-day is more particularly toward a single individual. The physician is dealing with patients who are already infected. That infection he can in no way eradicate. His duty is to maintain the forces of the patient until he himself has overcome the invader, and to protect him from further injury. The great difference, however, between the duties of the physician and the surgeon, lies in the fact that every one of the infected individuals is a source of danger to those about him, and it is the obvious and necessary duty of the physician to use every means in his power to prevent the spread of the disease from the individual who is under his care—not only to the special case in his immediate vicinity, but to the many unknown individuals who may be reached by the dissemination of the infectious agent.

But has the problem before the surgeon never been similar? Consider for a minute the story of hospital gangrene, once the infection was there, the condition was almost beyond relief, but by the application of antiseptic and aseptic methods the surgeon has done far more than save the individual case, he has eradicated the disease. How has he done this? Not only by the exercising of scrupulous cleanliness in his operative technique, but in the careful protection of his patient from any sort of association with an infected individual.

Let there be an instance of streptococcus infection in a surgical ward—how quickly 'tis removed to the isolating pavilion. "Ah, yes," says the objector, "this is true, but that case of streptococcus infection is a source of immediate danger to those about him, and if the infection spreads, it is almost certain to end in the death of one of the individuals who is under the special care of the surgeon. In the medical ward, however, contagion from typhoid fever or dysentery is not very likely, and if it does occur, the chances of a fatal issue are so very much less that it is not unnatural that such rigid precautions should not be taken."

This objection again has elements of truth, and contains, doubtless, the kernel of explanation as to why we physicians have been and are so careless in these matters. The main reason for our negligence is the relative infrequency of contagion—the relative mildness of the infection when it does occur. An occasional case of typhoid fever breaking out among nurses and physicians in a large hospital is passed almost unnoticed. We hardly realize until we look carefully into the matter that our own negligence is responsible for its development.

But there is another side of the question which lends a very grave aspect to the situation. The lack of proper antiseptic and aseptic precautions on the part of the surgeon is followed, as a rule, by evil results with regard to one individual alone,

or at the most to a few patients in his ward, or his own practice. The lack of antiseptic precautions on the part of the physician, in the care of a single case of typhoid fever, may, under proper circumstances, give rise to an explosive epidemic, followed by hundreds of deaths.

Regard it as we may, we must come to the painful conclusion that physicians as a body have been content to limit their practice to the treatment of infections after they have occurred, while the surgeon has long since passed beyond this, and has recognized that his most important duty lies in prophylaxis against this infection.

That it should be more natural for the surgeon to perceive and appreciate this duty from the character of his practice, in that negligence affects him more directly, may be true, but this detracts in no way from the great and important duty which lies before the physician—a duty with which, at the moment, he has hardly grappled.

What steps then, ought we to take? Some of us, I am sure, must feel like saying to ourselves, "Go to the surgeon, thou sluggard!" Indeed, we might do worse. The work must probably begin in the large clinics where such problems can best be attacked, where the example can best be set. What should we do? First, we should see to it that contagious diseases, such as pulmonary tuberculosis, typhoid fever and dysentery, should not be treated in the general wards.

1. There should be special typhoid wards, special tubercular wards and special isolating wards in which diseases such as bacterial dysentery may be cared for.

2. Precautions such as those now supposed to be taken in connection with typhoid fever should be taken in the care of patients with diseases such as pneumonia or influenza.

3. Orderlies and nurses with bad colds or tonsilitis should not be allowed to attend regularly to susceptible individuals or to those in whom the contraction of the malady might produce grave results, such, for instance, as patients suffering with mitral disease.

4. Every hospital ward should be thoroughly and effectively netted against flies and mosquitoes. The omission of a precaution so elementary in its necessity as this should be regarded as criminal negligence.

5. Not only nurses and orderlies, but attending physicians, should wear clean uniforms or gowns, whenever attending wards containing contagious diseases, and should remove them on leaving the wards. And among contagious diseases I include such maladies as typhoid fever, tuberculosis and dysentery.

6. All attendants should invariably and thoroughly wash their hands on leaving a ward or a bed containing a patient suffering with an acute infectious disease.

7. The observance of the necessary precautions of sterilization of the clothes, eating utensils, excreta and bath water of all patients with infectious diseases, should be as rigidly and thoroughly enforced as are the antiseptic rules in the surgical operating room.

8. Cultures should be taken from the urine and faeces of all typhoid patients before their discharge from the hospital and, as a rule, no patient should be discharged until his excreta are free from the infectious organism.

Similar steps should be taken with regard to dysentery.

If precautions such as these were uniformly adopted in our large hospitals, a great step would be taken, not only toward the immediate protection of the population of that institution and of the surrounding community, but toward the education of the medical and lay-public at large, for similar precautions should also be taken in connection with patients whom we are attending at their homes.

Suppose the patient be a sufferer from typhoid fever. The first step should be exactly that which was taken in the campaign resulting in the eradication of the epidemic of yellow fever from Havana, viz:

1. The house should be thoroughly netted. No flies from that patient should infect the food of his neighbors. Furthermore, when possible,

2. No one but the attendants should be allowed in the room of the patient.

3. If, however, it is necessary for one member of the family to be present, that individual should adopt all the precautions observed by physician and attendants.

4. The physician should wear a fresh, clean gown whenever he visits the patient. A sufficient supply of these garments should be kept, so that a fresh one may be worn at every visit. The gown should be placed immediately in a tin boiler and boiled after every visit of the doctor, so that in most cases one or two gowns would suffice.

5. The rules for the sterilization of the bath water, excreta, clothes, and eating utensils should be carried out in the same manner as in the hospital.

6. Final cultures should be made in the same way.

"Theorist and dreamer!" cries the objector. "This is all very well to talk about, but how about the expense and the time involved in such measures? Neither our shallow pockets nor our full days can suffice for such demands. This is a pleasing, but quite unrealizable fancy."

What a natural utterance! But reflect for a minute: What would the average surgeon of fifty years ago have said if one had suggested to him that, in the near future, it would be necessary to make the preparations which are now called for in connection with an ordinary surgical procedure—if one should have told him of the equipment required for the operating room—of the precautions of sterilization to be adopted with regard to instruments, ligatures, and indeed everything that touches the patient—if one should have suggested to him the preparations that the surgeon himself must make—the care of the hands, the costume, the gloves and the other minutiae connected with the preparation for an ordinary operation—if one should have assured him that all his wooden and tortoise shell instruments would be discarded in a few years as dirty and dangerous? If one had said these things to one of the best of surgeons fifty years ago, he would probably have regarded the individual who made such suggestions as a madman, and laughed at the absurdity of it all.

And one of his first objections might well have been the

enormous expense which such preparations would involve, and the utter impossibility of considering for a moment that such an extraordinary procedure should be practicable. And yet, to-day, we think of these preparations as a matter of necessity and duty and the man who fails to observe them is regarded as criminally negligent. Now procedures such as I have outlined are very far from being so elaborate or expensive as those which are recognized as wholly necessary in the surgery of to-day, and although the surgical antisepsis seems more urgent because of the immediate consequences of its non-observance, yet the neglect of proper medical antisepsis may mean, in any individual case, a result infinitely more serious.

The notorious and discreditable prevalence of typhoid fever in our country will continue until the time comes when we medical men and the public realize that it is to our carelessness, negligence and unclean habits that it is due. When we do realize this as a body, and when we attack the problem as our colleague, the surgeon, has done in connection with his branch of the healing art, then, and only then, can we begin to look forward to the day when we shall really control the prevalence of typhoid fever and similar infectious diseases as the surgeon has controlled wound infection.

This is but the beginning of the work that lies before us. I have not even touched upon the milk question—one of the gravest from the standpoint of public health—one toward which we physicians have been shockingly indifferent. Think again, of the conditions which exist among the poor and ignorant and of the scantiness of the measures which we adopt to-day to prevent the spread of typhoid fever by contagion, after all the lessons of the Spanish War and the admirable and illuminating studies of the German Health Bureau!

These problems must be dealt with by a thorough organization of our departments of public health—state, county and municipal—but the first step toward this end must be our insistence as individuals in each individual case on those measures which are necessary for the protection of the household and the public. Individual effort is the keystone of the prophylactic arch which spans the road to better days.

Let us turn now to another aspect of medical antisepsis—quite different from that which we have just been considering:

Some months ago a distinguished English physician said to me: "There is an immense amount of sepsis in medicine." To what, you may ask, did he refer? The observation was made in the course of a conversation upon the frequency with which small local foci of infection are overlooked—foci of infection which lie often at the root of grave general systemic disturbances—foci, which, of themselves, may produce little or no subjective, or, indeed, sometimes objective, disturbances. The speaker was referring especially to the anaemia and general debility which may be associated with the inflammatory processes occurring about teeth in interstitial gingivitis with tartar formation and the eventual development of pyorrhoea alveolarum—that common malady which may almost be regarded as an incident of advancing years, a condition to which few practitioners of medicine, and by no means all dentists, pay sufficient attention. It was indeed this casual remark which suggested to me the subject of my observations this evening.

Thorough oral antisepsis, particularly in regard to the gums, is a point of really great importance to which the physician, and indeed too often the dentist, pays far too little attention. The physician who insists that the patient with excessive tartar formation and bleeding gums place himself under the conscientious care of a competent dentist, will often be more than gratified to see the surprising effect upon the general health of the patient. More than this—he may avoid truly serious complications, for there can be no doubt that at times pyorrhoea and alveolar abscesses give rise to grave general results.

Let us then, for a moment, consider this aspect of sepsis and antisepsis in medicine:

The discovery of a local focus of infection which has been at the bottom of some puzzling general disturbance—anaemia, debility, fever, is an everyday occurrence in the practice of medicine—inflammatory disease of the adnexa in the pale, nervous woman who has made no complaint of local trouble—the chronic prostatitis or posterior urethritis or fistula-in-ano in man—the nasopharyngeal adenoids in the undeveloped, feeble child.

The variety of symptoms, however, which may result from such chronic foci of septic absorption is not always fully realized, nor is it generally understood that these local foci may really be difficult or even impossible to recognize in the course of the ordinary routine physical examination.

Again, it is interesting to note the frequency with which we have been in the habit of misinterpreting the significance of our own wise acts. The remarkable effect of removing nasopharyngeal adenoids on the development and growth of some children is an old story. The brilliant result, the transformation of a pale, feeble, dull youngster, with palpable glands in his neck and frequent unaccountable febrile attacks, into a healthy, robust child, is commonly attributed to the simple removal of a mechanical obstruction to respiration. As a matter of fact, however, this improvement is due in many, if not in most instances, to the elimination of a focus of chronic infection from which there has been a constant absorption of toxic substances and perhaps even of pathogenic micro-organisms.

That symptoms of chronic septic absorption from simple debility, languor, anaemia, and slight unaccountable febrile manifestations to sharp, intermittent fever, ague, arthritis, endocarditis and grave septicaemia, may be observed with chronic infections of the lymphatic tissue of the fauces and pharynx, is well known, but the frequency of such symptoms in the absence of any objective or subjective local manifestations is not so widely appreciated as might be desired.

'Tis especially to the work of J. L. Goodale, of Boston, that we owe our increasing knowledge of the importance of local disease of the upper respiratory tract as a cause of general systemic disturbance.

The first and main point upon which I would insist is the importance of a thorough investigation by a competent laryngologist of the faucial and pharyngeal tonsils in all cases of

general systemic disturbance, the cause of which is obscure. We are prone to pass by without consideration tonsils which are small and appear clean on the surface, forgetting or ignoring the fact that often enough 'tis the small buried sclerotic tonsil with crypts narrowed or closed at their orifices which is the most serious menace to the possessor. Such tonsils, mere shells filled with cheesy or purulent contents, are often associated with exceedingly grave general disturbance.

What a variety of manifestations may occur with unsuspected tonsillar infections may be illustrated by a few of my own experiences.

1. A young woman of 29 had been subject for two years to unaccountable febrile attacks which had finally led to a slight, regular, daily, evening rise of temperature. There were frequent "colds" and a rather annoyingly persistent cough. Tuberculosis was suspected, and the patient was sent to a sanitarium where she spent several months. The fever continued. Physical examination of the chest was wholly negative. The pelvic organs were free from disease. On inquiry it was found that there had been several attacks of tonsilitis in the preceding six years. The tonsils, not remarkable on superficial examination, were found to be badly diseased. Their removal was followed by the immediate disappearance of fever and a rapid return of good health.

2. A young woman of about 25 had had for nearly six months slight evening fever with debility and loss of weight. Her physician, suspecting tuberculosis, had put her under a rigid rest and open air treatment, during which, after several months, she had gained much weight, and the fever had disappeared. She had not had tonsilitis for at least ten years. The tonsils were rather large, the surface glazed, the crypts evidently closed; small pin-head yellowish spots were seen beneath the mucosa. On removal, they were found to be badly diseased. Moreover, the naso-pharynx contained a large cyst full of foetid cheesy and calcified material. In neither of these cases were the tonsils tuberculous.

3. A boy of twelve had been subject for several years to unaccountable febrile attacks with nausea, headache and general aching pains. Two weeks before I saw him one of these attacks was associated with transient albuminuria. There was *no history of tonsilitis.* The tonsils were, however, large and evidently diseased. Their removal was followed by immediate recovery—no return of albuminuria or fever.

4. A boy of seven had had for some months frequent, often daily, attacks of fever, accompanied by chills in the late afternoon or evening. There was marked emaciation and debility. His father, a physician, suspected tuberculosis—*no history of tonsilitis.* The tonsils, not remarkable on superficial examination, were found to be badly infected and on the day of their removal the fever disappeared. A year later, recurrence of chills and fever. On examination, it was found that a small island of lymphatic tissue which had been left had become hyperplastic. A single rather deep crypt had become infected and closed, forming a cyst containing pus. The fever disappeared upon its removal, and the boy has remained well now for nearly two years.

5. A young man of twenty-four had had in five years several attacks of sub-acute arthritis, which, at one time, was regarded as arthritis deformans. He had had hydrotherapeutic treatment at Wiesbaden and had been advised to repeat the course of baths every summer. Last summer, recurrence of the arthritis. *No history of tonsilitis.* The tonsils were, however, badly infected and since their removal last June he has been quite well. No recurrence of the arthritis.

6. Boy of eighteen; for a year, weakness, debility, slight albuminuria. *No history of tonsilitis.* The tonsils did not appear to be enlarged, and were apparently clean. On examination they were sclerotic, atrophic and filled with retained material. Removal resulted in complete recovery with disappearance of the albuminuria.

7. A young woman of twenty-three. For three years, general debility and loss of 27 pounds. Aching sensation in throat. No knowledge that she had had tonsilitis. Trace of albumin and hyaline casts in the urine. Tonsils small and apparently clean, but on examination found to be sclerotic and badly infected. Two weeks after removal the patient was much better; the urine free from albumin. Four months later the urine was still clear and the patient in excellent general condition. Eight months after this the patient reported that she had gained thirty-five pounds in weight.

8. A lady about forty-five years of age was seized last June with a rather sudden high fever and marked prostration. The condition was regarded at first as influenza. There was a well marked leucocytosis, no local symptoms—continued fever with exacerbations. The throat was rather injected; there was no tonsillar enlargement, and no complaint relative to the throat. In the absence of any evident cause for the fever, Dr. Bordley was requested to make a special examination of the tonsils, which revealed a small abscess of the left tonsil, which broke during the examination. The temperature fell almost immediately. Complete recovery followed. There were absolutely no local subjective symptoms.

9. A woman of about 35; ten years before slight haemoptosis, followed by a long continued, slight, regular evening fever, for which she had been under treatment, at a sanatorium, for tuberculosis. In the fall of 1908 there developed again an unaccountable regular slight evening rise of temperature to a point about 100° F. or a little under. Repeated physical examination revealed no local cause for the fever. There was no cough. The patient, the wife of a physician, was kept at absolute rest, in bed, in the country, for nearly six months. In the early summer of 1909 partial hemiplegia, associated with symptoms on the part of the nervous system, which suggested to her physician a possible disseminated sclerosis. An examination of the tonsils, of which there had been no complaint, showed marked disease. A thorough emptying of the infected crypts resulted in immediate disappearance of the fever and rapid improvement in the general condition and complete disappearance of all symptoms relative to the central nervous system. In the course of a month there was a slight recurrence of the fever which disappeared again on a thorough cleaning of the tonsil-

lar crypts, which had refilled. Removal of the tonsils in the fall of 1909 was followed by complete and permanent recovery.

This patient had no evidence elsewhere of arterial disease, and the cerebral symptoms have been attributed by all who followed the case to an infectious arteritis. I had seen this lady on various occasions during the fall of 1908 and the spring of 1909. I had examined her tonsils, raised the question of a possible infection, and dismissed it.

In not one of these cases was the patient aware that there was any tonsillar infection. In many, the ordinary routine examination suggested little or nothing. In all, however, the infection in faucial or pharyngeal tonsils was at the root of more or less grave general disturbances—arthritis, endocarditis, anaemia—debility, albuminuria, suspected tuberculosis, cerebral thrombosis.

Ten years ago I am sure that I should have passed over many of these cases. While the tonsils, faucial and pharyngeal, are perhaps the commonest seats of cryptic infection, the careful observer will, however, be considerably surprised to find how often in chronic conditions of debility, anaemia, arthritis, slight unaccountable persistent fever, unsuspected disease of some one of the sinuses, ethmoidal, sphenoidal, frontal, may be found, the proper treatment of which will have a striking effect upon the general health of the patient and perhaps on other local manifestations which at first glance would seem to be quite unconnected with it.

The importance of the removal of such foci in chronic deforming arthritis has been much emphasized of late, but it is not only in cases of arthritis, acute or chronic, or marked febrile disturbances, that one should look for larval infections, but also in every otherwise unaccountable condition of debility.

The discovery and removal of badly infected tonsils while the symptoms are yet but slight, may save the affected individual from a fatal endocarditis or a deforming arthritis, or a chronic nephritis. The early detection and treatment of interstitial gingivitis may not only save the teeth, but may perhaps, if we are to believe the teachings of Hunter, prevent the development of a fatal Addisonian anaemia.

The cursory consideration of this phase of sepsis and antisepsis in internal medicine leads us to realization of how much truth there was in the observation of our English colleague of whom I have spoken. There *is* an immense amount of sepsis in medicine, and one of the most important of our duties is to suspect it, to seek for it, and not to tire until we have found it. If we search conscientiously we shall find it, sometimes, where we least expect it, and in so doing we shall perform another of the great prophylactic duties of our art.

Let us emulate our colleague, the surgeon, in our methods of antisepsis in relation to contagious diseases in the broadest sense of the word, and let us further recognize the frequency with which small foci of infection are responsible for grave general symptoms, and the importance of their early recognition and elimination.

Principiis obsta, sero medicina paratur.

THE SEWERAGE SYSTEM OF THE CITY OF BALTIMORE.[1]

By Calvin W. Hendrick,

Chief Engineer of the Sewerage Commission, Baltimore.

The sewerage system is about half completed, and we are within our estimated time and cost.

We will begin the actual use of the sewerage system the latter part of this summer, by beginning to connect up houses in East Baltimore along the high level interceptor.

There is one fact I would like to impress on the citizens of Baltimore, viz.: that the present $10,000,000 sewerage loan was voted on and passed before the present Sewerage Commission came into existence. The present Commission, therefore, is not responsible for having to ask for an additional loan. We have never made but one estimate or one statement as to cost and time of completion, as outlined in our 1907 report, as follows:

> With the aid of the information now at hand, I feel safe in saying that the cost of the sanitary sewers outlined in the Commission's Report for 1906 will be about $14,000,000, based upon present prices and the assumption that it will be possible to push the work vigorously. If for any reason the work should be delayed, an increased allowance would have to be made for salaries, office rent and other expenses. If the work is vigorously prosecuted, it is believed that the sanitary sewers as laid out in the Commission's Report for 1906 can be fully completed by the year 1914. The entire storm-water system, as outlined in the Commission's Report for 1906, can probably be constructed for about $4,500,000.

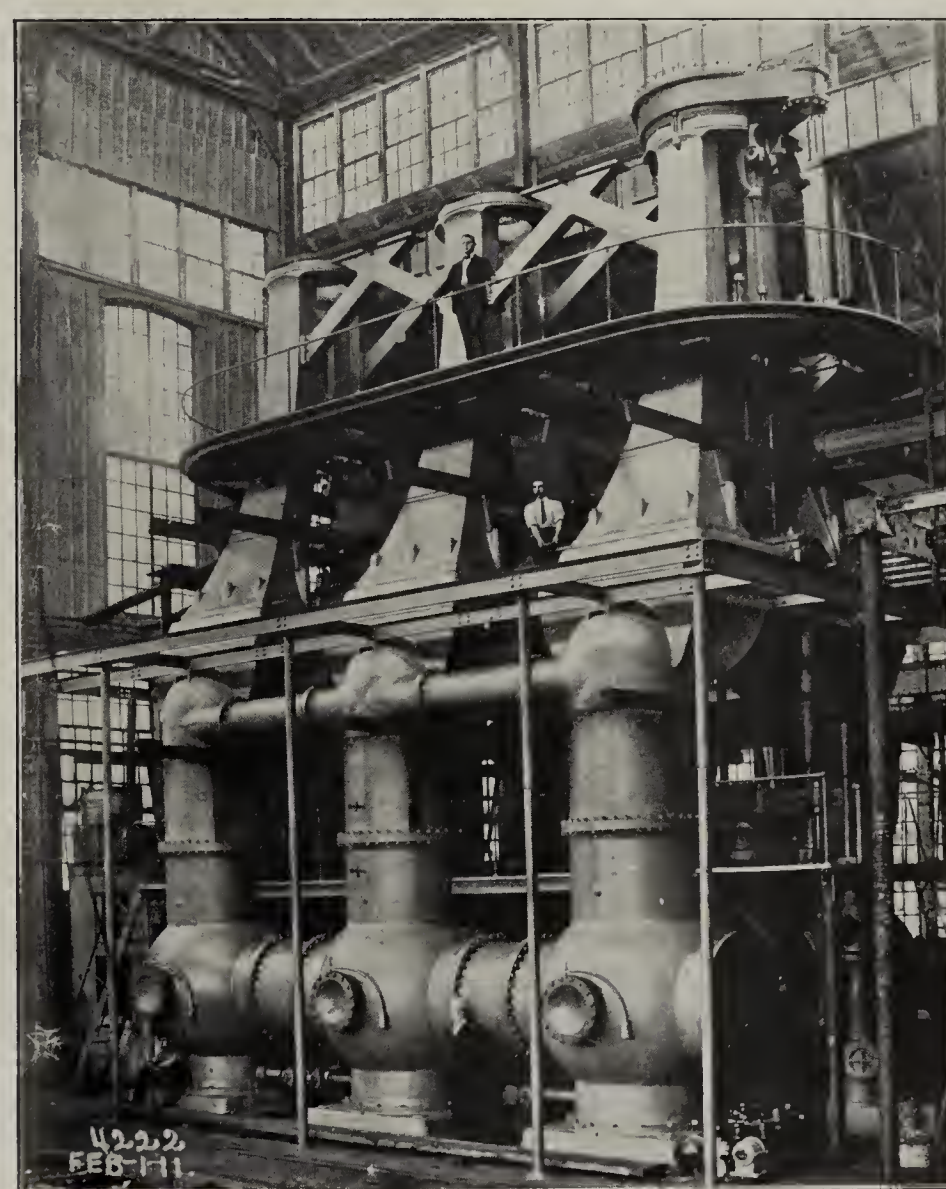
On account of the low rate of interest paid on the bonds, the city was obliged to sell the first loan at $516,529.83 less than its face value, leaving only $9,483,470.17 available for the work.

Unless one takes the time to visit in person some of the construction work being carried on in various parts of the city by the Sewerage Commission, you cannot realize the magnitude of the work nor the diversified engineering problems that are being solved every day. The people outside of Baltimore seem to appreciate this more than do the citizens of Baltimore, from the fact that we have more visitors from outside (some having traveled thousands of miles), than we have from the people living in Baltimore. These foreign visitors are not the merely idle or curious, but are citizens of consequence and engineers who are doing things throughout the world.

[1] Notes of a paper read before The Johns Hopkins Hospital Medical Society, October 16, 1911.

VIEW FROM WATER TOWER OF HYDROLYTIC AND SLUDGE DIGESTING TANKS, AND SPRINKLING FILTERS WITH SETTLING BASINS SHOWN IN THE DISTANCE
BACK RIVER DISPOSAL WORKS

AUTOS IN OUTFALL SEWER AT JUNCTION OF THE HIGH LEVEL INTERCEPTOR AND THE FORCE-MAIN SEWER



ONE OF THE FIVE 27,500,000 GALLON PUMPING ENGINES, No. 1

Our work is most interesting on account of its complications. I will endeavor to give you a slight idea of its magnitude and difficulties. We will start on the supposition that water must flow down hill. This means that an 8-inch sewer, beginning at Forest Park, 13 miles distant from the disposal plant, must continue on a constantly falling grade, which cannot be flattened beyond certain rates, ever increasing in size as sewers lead into it from valleys and hills covering an area of 32 square miles, in its path, crossing Peck's Branch, the B. & O. tunnel, over and under Jones' Falls, the Pennsylvania tunnels, crossing over ravines, swinging around hills, tunneling through ridges, passing through narrow alleys, by the side of tall buildings, ever continuing on the constant falling grade; ever increasing in size until, on reaching the disposal plant, it is large enough to contain two automobiles, one on top of the other.

Two-thirds of the sewage of the city is intercepted and carried to the disposal plant by gravity; the other third is lifted by enormous pumps, each with a capacity of 27,500,000 gallons a day, from a point 13 feet below tide to the outfall sewer, a height of 72 feet (including friction), an unusually heavy lift, especially as sewage is much more difficult to pump than water. Three of these enormous pumps are constructed and are now being installed. The pumping station is large enough for two more, to be installed later. The foundations for these pumps have been so constructed, independent of the foundations for the building, as to absorb all shocks.

The difficulty of our work is doubled on account of having to construct two systems of sewers and drains, crossing and recrossing each other in a thousand different places. The reason for the necessity of having to construct two systems is that the legislature requires every gallon of sewage to be taken into the sanitary system, to be purified before discharging it into the Chesapeake Bay or its tributaries. It is therefore of the utmost importance that we reduce the amount of sewage to be pumped and treated to a minimum, in order to keep down the size of the sewers, the pumping plant, the disposal plant, and the unnecessary constant treating and pumping of clean rainwater. To attempt to treat all the rain that falls would break a city. Therefore, the sanitary sewers will take care of the drainage from bath tubs, kitchen sinks and toilets, the rainwater will pass off through the storm-water drains, by inlets at the corners.

Now, to attempt to install these two systems of drains and sewers in the beds of streets of a city over a hundred years old, in which a mass of pipes have been laid, but in which practically no space for sewers or drains has been left, brings us face to face with a serious problem, and these sewers and drains must continue on ever-descending, regular grades and cannot twist over and under obstructions like water pipes, gas pipes and other public structures.

If the sewers could be laid in the streets it would simplify matters, but as far as we can we are attempting to lay them in the alleys, which are very narrow. Unless you have had experience in building a sewer in a narrow alley, having a constant surface flow from kitchen sinks and bath tubs, lined with old brick buildings on shallow foundations, in bad condition, with leaking water pipes and sewers under the surface, you cannot realize the difficulties we have to overcome. In the low section around the harbor the troubles are even greater, as the sewers are below tide level.

The constant accumulation of ice in these alleys, caused by this surface flow, will be entirely eliminated when the sanitary sewers are constructed. The constant trickling flow in cold weather causes a rapid accumulation of ice.

The city is getting its sewers constructed for almost cost, on account of the wholesale prices secured by the manner in which we have extensively advertised and let the contracts, doing a great part of the work by machinery, which is the proper way to get low prices.

There has been completed, the outfall sewer, extending from Chase and Durham Streets to the disposal plant at Back River; the high level interceptor to Jones' Falls; the Jones' Falls sanitary interceptor, paralleling the east side of Jones' Falls, passing under the new Union Station, and crossing Jones' Falls at North Avenue, extending through McMechen and Laurens Streets to Druid Hill Avenue; the force-mains and the force-main sewer, from the outfall sewer to the pumping station at Eastern and East Falls Avenues; the east low level interceptor, from the pumping station to Boston and Hudson Streets; the west low level interceptor, from the pumping station through President, Pratt, Light, Hill, Sharp, Ostend and Warner Streets to Alluvion Street. The majority of the sanitary laterals in East Baltimore have been laid in the streets to the curb lines. The pumping station is practically completed, with the roof on, and the chimney half way up. The interceptors and pumping station are built for a million people.

In addition, a disposal plant and sanitary system is in operation covering a large part of Walbrook. Another disposal plant, with trunk sewers, covering a large section in the northwestern part of the city, is in operation.

The sewers completed and under contract, about 160 miles, if placed end to end would almost reach from Baltimore to New York, a portion of which are large enough to drive through in automobiles.

The Sewerage Commission will extend the sewer connections up to the property or building line, either front or rear, making the expense to the property holder of connecting up with the sewerage system a small one.

I feel safe in stating that the entire built-up portion of the city will be completely sewered and in operation in 1914, the time originally stated, provided we are allowed to continue in the rapid manner we have so far prosecuted the work.

The public has little conception of the extensive and urgent relief the installation of the storm-water drains is bringing to the city by preventing flooding, eliminating thousands of objectionable cross gutters, improvement of property, etc. If the present Commission had done nothing more than bring about the improvements caused by the building of the storm-water drains and the covering in of Jones' Falls, eliminating this great nuisance, it would have performed a great and lasting

service to the city. But the storm-water proposition is only a side issue compared to the sewering of the city.

The disposal plant is constructed on the unit system, in order that it may be added to as the sewers are gradually extended. The number of units at present drawing to completion are sufficient to purify the sewage of about 275,000 people, or that portion of the city which will be sewered under the present loan.

The method of treating the sewage is as follows:

At the mouth of the outfall sewer will be installed screens that will catch such things as sticks, rags, etc., which will be removed and burned. The sewage will then pass through the meter house, which will measure its flow; then through hydrolytic tanks, about 450 feet long, requiring 8 hours for passage, a sufficient length of time to allow the solids to settle, the liquid passing on to an intercepting channel, to and through what we call the gate-house which distributes it to the stone sprinkling filters, located at a level 15 feet below the hydrolytic tanks, giving a hydraulic head of sufficient force to spray the sewage over these stone beds through nozzles or jets, spaced 15 feet apart. The hydraulic head will be controlled by butterfly valves, causing the sprays to rise and fall, varying from close to the nozzles out to the limit of 15 feet, thus utilizing the entire surface of the stone bed, a large portion of which would be wasted if the sprays were stationary. These nozzles will throw a square spray, thereby saving additional space which would be lost if the sprays were circular, as you know where circles touch there is a lost triangle.

The spraying of the sewage through the air is essential to the aeration and purification of the sewage. As the sewage falls on these beds it trickles down through 8½ feet of broken stone varying in size from 1-in. to 2½-in. The passing of the sewage through these beds forms a gelatine-like film on the stones, in which certain bacteria multiply by the million, attacking and killing the injurious bacteria in the sewage. We therefore make the bacteria do the work for us by fighting each other. The sewage on reaching the bottom of these stone beds is practically pure, and is then carried by intercepting channels leading to a central channel under the stone beds, which finally delivers the purified sewage to the settling basins, requiring three hours to pass through. These settling basins are not for the purpose of causing additional purification, but to clarify the fluid, as there are certain mineral substances in the sewage which the bacteria do not annihilate, such as is found in the Mississippi River water, which is muddy but not injurious to drink. The sewage then passes with a drop of 18 feet through the power house, in which turbines are placed, operated by the flow of the sewage. They in turn run dynamos which generate electricity, giving us power to light the plant, run the sludge pumps and lift the clarified sewage to a water tower for flushing purposes.

In other words, by the simple gravity flow of the sewage it is purified, and power is obtained to light and run the plant at practically no cost.

It all comes down to the fact that we are getting nearer to the laws of God than ever before, which laws man cannot improve on, but can only strive to follow. For instance:

The pumps lifting the sewage from the low level to the outfall sewer, is the sun drawing the salt water from the sea to the cloud; the flow of the sewage through the outfall sewer to the disposal plant, is the cloud drifting through the air; the spraying of the sewage over the stone beds is the rain falling from the cloud to the earth; the trickling of the sewage down through the stones is the rain sinking into the earth; the purified sewage coming out into the settling basins is the spring water bubbling out of the ground, and the electric light produced by the flow of the sewage is the sunshine after the clouds have passed.

NOTES AND NEWS.

Dr. Walter A. Baetjer is Acting Resident Physician, Bay View Hospital, Baltimore.

Dr. Montague Boyd is Clinical Assistant in Surgery, Atlanta College of Physicians and Surgeons, and Andrologist, The Wesley Memorial Hospital, Atlanta, Ga.

Dr. J. R. B. Branch is Attending Gynecologist to the Macon Hospital and Instructor in Gynecology and Obstetrics, the Macon Hospital Training School for Nurses. Address: 673 Cherry Street, Macon, Ga.

Dr. John R. Caulk is Instructor in Genito-Urinary Surgery, Washington University, Associate Genito-Urinary Surgeon to Mullanphy Hospital and Genito-Urinary Surgeon to Bethesda Hospital. Address: Humboldt Building, St. Louis, Mo.

Dr. T. Wood Clark is Attending Pediatrist, Faxton Hospital, Utica, N. Y. Address: 240 Genesee Street, Utica, N. Y.

Dr. Calvin D. Cowles, Jr., is Captain Medical Corps, U. S. A. Address: West Point, N. Y.

Dr. Ernest S. Cross is Physician in Charge, Aiken Cottage Sanatorium, Aiken, S. C.

Dr. J. McPheeters Glasgow is Professor of Materia Medica and Therapeutics, Medical Department of Vanderbilt University, and Visiting Surgeon to St. Thomas Hospital. Address: The Worthington, Nashville, Tenn.

Dr. Robert L. Cunningham is Instructor in Clinical Medicine, Los Angeles Medical Department, University of California, Chief of Medical Clinic, Selwyn Emmett Graves Dispensary, Attending Physician, Los Angeles County Hospital and Attending Physician, Barlow Sanitarium, Los Angeles, California.

Dr. Joseph Erlanger is Professor of Physiology, Washington University, St. Louis, Mo.

Dr. W. L. Estes, Jr., is Chief of Staff, St. Luke's Hospital, South Bethlehem, Pa.

Dr. F. Webb Griffith is Surgeon to the Biltmore Hospital, Asheville, N. C.

Dr. Runkle F. Hegeman is a member of the Staff of the New York Foundling Hospital, New York City.

Dr. Charles W. Hennington is Assistant on the Staff of the City Hospital and Surgeon to the Rochester State Hospital, Rochester, N. Y.

Dr. W. H. Higgins is Instructor in Clinical Medicine, University College of Medicine, Richmond, Va. Address: 101 W. Grace Street, Richmond, Va.

Dr. Gerry R. Holden is Gynecologist to St. Lukes Hospital, Jacksonville, Fla. and Gynecologist to the Florida State Hospital, Chattahoochee, Florida. Address: 215 Laura Street, Jacksonville, Fla.

Dr. J. Gardner Hopkins is Assistant in Clinical Pathology, Columbia University, Bacteriologist, St. Luke's Hospital, and Pathologist, Sloane Hospital for Women. Address: 350 Washington Avenue, Brooklyn, N. Y.

Dr. Henry M. Hurd has resigned his position as Superintendent of the Johns Hopkins Hospital, and has been appointed Secretary to the Board of Trustees.

Dr. Henry T. Hutchins is Fellow in Gynecology, The Harvard Medical School, Surgeon to Out Patients, The Free Hospital for Women, Brookline, Mass., and Consulting Gynecologist to the Rufus S. Frost Hospital, Chelsea, Mass., and to the Memorial Hospital, Pawtucket, R. I. Address: 374 Marlborough Street, Boston, Mass.

Dr. Clarence B. Ingraham is Instructor in Obstetrics and Clinical Assistant to the Gynecological Department, University of Colorado, and Obstetrician to St. Luke's Hospital, Denver. Address: 1405 Glenarm Place, Denver, Colo.

Dr. C. R. Kingsley is Pathologist and Dispensary Physician, S. R. Smith Infirmary, Staten Island, and Pathologist, St. Vincent's Hospital, Staten Island. Address: 305 Jewett Avenue, West New Brighton, N. Y.

Dr. Irwing P. Lyon is Lecturer on Clinical Medicine, University of Buffalo, Librarian, Medical Department, University of Buffalo, Assistant Attending Physician, Buffalo General Hospital, and Consulting Physician, Dispensary for Tuberculosis, Charity Organization Society.

Dr. W. G. MacCallum is Director of the Pathological Department, Presbyterian Hospital, New York.

Dr. J. D. Madison is Professor of Medicine, Wisconsin College of Physicians and Surgeons, and Attending Physician to the Milwaukee County Hospital and St. Joseph's Hospital.

Dr. E. M. Mason is Pathologist to the Hillman Hospital and Physician to the Jefferson County Anti-Tuberculosis Camp and Dispensary. Address: Empire Building, Birmingham, Ala.

Dr. G. Brown Miller is Associate in Gynecology, the George Washington University, Gynecologist to the Garfield and Emergency Hospitals, and Associate Gynecologist to the Columbia Hospital and to the George Washington University Hospital, Washington, D. C.

Dr. Roger S. Morris is Associate Professor of Medicine, Washington University Medical School, St. Louis, Mo.

Dr. Douglas H. Morse is Resident Pathologist, Washington University Hospital, Saint Louis, Mo.

Dr. Charles C. Norris is Instructor in Gynecology, University of Pennsylvania, Attending Physician to the Maternity Hospital, and Assistant Gynecologist and Obstetrician to the Philadelphia General Hospital. Address: 1503 Locust Street, Philadelphia, Pa.

Dr. Francis W. Peabody is Assistant Resident Physician, Hospital of the Rockefeller Institute, New York City.

Dr. Frederick S. Ray is Clinical Assistant in Surgery, Los Angeles Department, College of Medicine, University of California. Address: 121 N. Union Avenue, Los Angeles, Cal.

Dr. E. H. Richardson is Visiting Physician to the Union Protestant Infirmary, the Church Home and Infirmary and the City Hospital at Bay View.

Dr. Thedore F. Riggs is Attending Surgeon, St. Mary's Hospital, Pierre, S. D., and Visiting Surgeon, Onida Hospital, Onida, S. D.

Dr. Stephen Rushmore has been appointed Consulting Gynecologist to the Symmes Arlington Hospital, Arlington, Mass. Address: 407 Marlborough Street, Boston, Mass.

Dr. S. W. Schaefer is on the Gynecological Staff of the Multnomah County Hospital, and Clinical Attendant in Surgery, the Free Dispensary. Address: 1022 Selling Building, Portland, Oregon.

Dr. John A. Sampson is Professor of Gynecology, Albany Medical College, and Gynecologist to the Albany Hospital and South End Dispensary.

Dr. Benjamin R. Schenck is Junior Attending Gynecologist, Harper Hospital, and Consulting Obstetrician, Woman's Hospital, Detroit, Mich.

Dr. Laurence Selling is Voluntary Assistant in the Königliche Psychiatrische und Nervenklinik, Breslau, Germany.

Dr. W. T. Shallenberger is Assistant in Clinical Gynecology and Obstetrics, Atlanta College of Physicians and Surgeons and Chief of Cystoscopic Clinic, Florence Crittenton Home, Atlanta, Ga.

Dr. Joseph T. Smith is Assistant Gynecologist, Lakeside Hospital Dispensary. Address: 628 Rose Building, Cleveland, Ohio.

Dr. Winford H. Smith is Superintendent of the Johns Hopkins Hospital.

Dr. Harvey B. Stone is Professor of Surgery, the Baltimore Medical School and member of the Staff of the Church Home and Infirmary.

Dr. S. A. Strouse is Associate Pathologist, Michael Reese Hospital, Chicago. Address: 3914 Ellis Avenue, Chicago, Ill.

Dr. Douglas Vanderhoof is a member of the Adjunct Faculty, Medical College of Virginia, Attending Physician to the Memorial Hospital and Consulting Physician to the Johnston-Willis Sanatorium, Richmond, Va.

Dr. Louis M. Warfield is Assistant Professor of Medicine, College of Physicians and Surgeons, Milwaukee, and Assistant Professor of Pathology, Marquette University Medical Department, Milwaukee, Wis.

Dr. Otis B. Wight is Adjunct in Gynecology, Medical Department, University of Oregon. Address: 608 Medical Building, Portland, Ore.

Dr. Gordon Wilson is Professor of Clinical Medicine, the University of Maryland, Baltimore, Md.

ARMY MEDICAL CORPS EXAMINATIONS.

The Surgeon General of the Army announces that preliminary examinations for the appointment of first lieutenants in the Army Medical Corps will be held on January 15, 1812, at points to be hereafter designated.

Full information concerning these examinations can be procured upon application to the "Surgeon General, U. S. Army, Washington, D. C." The essential requirements to securing an invitation are that the applicant shall be a citizen of the United States, shall be between 22 and 30 years of age, a graduate of a medical school legally authorized to confer the degree of doctor of medicine, shall be of good moral character and habits, and shall have had at least one year's hospital training as an interne, after graduation. The examinations will be held concurrently throughout the country at points where boards can be convened. Due consideration will be given to localities from which applications are received, in order to lessen the traveling expenses of applicants as much as possible.

The examination in subjects of general education (mathematics, geography, history, general literature, and Latin) may be omitted in the case of applicants holding diplomas from reputable literary or scientific colleges, normal schools or high schools, or graduates of medical schools which require an entrance examination satisfactory to the faculty of the Army Medical School.

In order to perfect all necessary arrangements for the examination, applications must be complete and in possession of the Adjutant General at least three weeks before the date of examination. Early attention is therefore enjoined upon all intending applicants. There are at present sixty-four vacancies in the Medical Corps of the Army.

NOTES ON NEW BOOKS.

International Clinics, Vol. II, Twenty-first Series, 1911. Price $2.00. (*Philadelphia and London: J. B. Lippincott Company.*)

Mobility and Malpositions of the Heart by SATTERTHWAITE, Chronic Cystitis in Women by BEYEA, Diseases Produced by B. Coli Communis by TURCK, The Progress of the Tuberculosis Campaign in Pennsylvania up to 1911 by FLICK and The Cultivation of Medicinal Plants by ALICE HERKEL are some of the many interesting papers in this volume. The variety of the articles makes the "Clinics" welcome to a large body of general practitioners who can find both amusement and information in them.

The Care of the Baby. BY J. P. CROZER GRIFFITH, M. D., Clinical Professor of Diseases of Children in the University of Pennsylvania. Fifth Revised Edition. Illustrated. $1.50. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

This book is so well known, and has proven so satisfactory to the profession and laity for more than fifteen years that this last edition needs no more than a mere word of welcome which we gladly offer it. It is a pleasure to see a book pass through numerous editions, as this at once stamps it as superior.

A Manual of Diseases of Infants and Children. BY JOHN RUHRÄH, M. D., Clinical Professor of Diseases of Children, College of Physicians and Surgeons, Baltimore. Third Revised Edition. Illustrated. $2.50. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

This excellent little manual requires no commendation from us. It has already proved its value, and in its revised form will undoubtedly be even more welcome than its predecessors. The author has been conscientious in his revision, and the book has been bettered. Many of the illustrations are excellent, others less good and poorly reproduced so that they do not stand out sharply. In the next edition we hope they will all be as good as the best.

A Text-Book of Medicine. BY DR. ADOLF V. STRÜMPELL. Edited by Herman F. Vickery and Philip Coombs Knapp. Two volumes. (*New York and London: D. Appleton & Co., 1911.*)

When a work has gone through seventeen editions there seems at first little for the reviewer to do beyond noting this fact and uttering a few platitudes. However, in this case it seemed worth while to do otherwise and make more than a cursory examination. The present is the fourth American edition and is edited by Drs. Vickery and Knapp of Boston. The work is in two volumes, which is certainly an advantage as the one volume modern text-book of medicine has grown to so great a size as to be difficult to handle. The two volume arrangement gives the opportunity of adding a section on mental diseases, which adds to its value. In general this work of Strümpell is a noteworthy one and has long held a foremost place among the text-books of the world. The descriptions of disease are clear and concise throughout with a proper balance held as to the amount of space given to each department. The section on diseases of the nervous system is particularly good and is fuller than in the majority of text-books.

The general character of the work being of the highest it is well to turn to a more special examination to find how accurately it has been brought up to date. There is room for a considerable criticism here and it is evident that Professor Strümpell does not keep up with modern literature. The section on the results of attempts to convey typhoid fever to animals takes no account of work for nearly ten years past and the successful results with monkeys are quite ignored. The discussion of typhoid perforation is wholly inadequate. For a modern work to advise the administration of opium as the main treatment of intestinal perforation in typhoid fever is disgraceful—there is no other word. The surgical treatment gets a line and a half and the statement that "experience of this is scanty" is not correct. There is very little attention devoted to the prophylaxis of typhoid fever and the statements about the results of vaccination ("have not led to any definite results") might have been sufficient some years ago but are not true to-day—this edition is dated 1911. Then on page 115, that miserable designation of Typho-Malarial Fever is brought in, for which the American editors are apparently responsible. Surely it is time that this term found oblivion and it is disappointing to find it perpetuated in such a work as this.

Under Epidemic Cerebro-Spinal Fever it is surprising to find that the work of Flexner is apparently quite unknown to the author both as regards the animal work and the serum. The editors might have been expected to correct this but they give only a very brief note of the results of the use of Flexner's serum without any mention of the method of its employment. This seems a serious omission. One always turns with interest to the discussion of the treatment of appendicitis. Of course there is much difference of opinion regarding this but it is disappointing to find so much stress laid on the giving of opium. The discussion of operation deals a good deal with the question of abscess formation and this quotation throws considerable light on the views held: "The physician must ask himself every minute whether further symptomatic treatment is permissible, or whether it may not be necessary to have the abscess opened by surgical interference." This is in the general discussion and not in reference to the treatment of cases with abscess. The rules given for operation do not seem very satisfactory, for example to place much reliance on elevation of temperature as an indication does not seem good practice when we remember that many of the most dangerous cases have little or no fever. The cases with early gangrene or perforation do not receive proper discussion and yet they are the most serious.

While we regard this text-book as one of the best, yet it is very evident from the few special points which were chosen for examination that the present edition cannot be regarded as having been brought up to date. There are many serious omissions which lessen its value. Professor Strümpell might be expected to have noted some of them but, whether or not, it seems reasonable to consider that the editors should have gone more carefully over recent work, particularly in American medicine.

Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India.

No. 43 (New Series). The Relation of Tetanus to the Hypodermic or Intramuscular Injection of Quinine. BY LIEUTENANT-COLONEL SIR D. SEMPLE, KT., M. D., etc. Price 1/2.

No. 44 (New Series). The Preparation of a Safe and Efficient Antirabic Vaccine. BY LIEUTENANT-COLONEL SIR D. SEMPLE, KT., M. D., etc. Price 9d.

Issued under the authority of the Government of India, by the Sanitary Commissioner with the Government of India. (*Simla-Calcutta: Superintendent Government Printing, India, 1911.*)

There is much in this series of "Scientific Memoirs" which is valuable, but many of the reports are very technical in character and can find but few readers, which is true of both the last which have just been received. Lieut.-Col. Semple's paper on the Relation of Tetanus to the Injection of Quinine would seem to have little practical value, unless it be that tetanus follows such injections more often in India than elsewhere. This can

only be due to an avoidable contamination, and the value of such a study as the author's appears problematical. His second report, like the first, is based on a series of carefully tried experiments, and is of greater importance, since rabies is a disease which may occur almost anywhere, and since all established, and proposed Pasteur institutes will be glad to have additional information as to the preparation of antirabic vaccine.

Hospital Management. A Handbook for Hospital Trustees, Superintendents, Training-School Principals, Physicians and all who are actively engaged in promoting Hospital work. Illustrated. Edited by Charlotte A. Aikens, author of "Hospital Training-School Methods and the Head Nurse," "Primary Studies for Nurses," etc. $3.00. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

Miss Aikens has gathered together an interesting and instructive body of papers on hospital management written for the most part by persons who have had practical experience in the problems which arise in such institutions. As the chapters are written by individuals who had no means of knowing the contents of any papers but their own it is not strange that some repetitions are to be found and undoubtedly the vigilant care of the editor has eliminated many which might otherwise have been present.

The subjects discussed are of great importance and ought to interest every hospital officer and trustee. Take as an example the paper of Dr. Metcalf on the "Purchase and Economic Use of Surgical Supplies." Here we have careful and detailed information under the head of dressings as to gauzes, bandages, absorbent cotton, plaster of Paris, iodoform gauze, cotton sheeting, cotton wadding and adhesive plasters with directions as to the best manner of procuring or making these. In rubber goods we are told what sort of rubber gloves to purchase and how to keep them in repair; also about hot-water bags, ice bags, drainage tubing, rubber tissues and the methods of preserving them from wear and deterioration. The difficult question of stomach tubes, catheters, bulb-syringes, air-cushions and atomizers is also fully touched upon. The various forms of suture material as catgut, silkworm gut, kangaroo tendon, etc., are described. The preparation of sterile sutures is not described nor the use of silver wire sutures, which one can but regard as a serious omission. Under the head of glass-ware we have clear and sensible recommendations as to the purchase of clinical thermometers, blood-counters, cover glasses and slides. Similar detailed information is also given as to anaesthetics, disinfectant solutions, splints, crutches and the like. This chapter is an example of many other similar chapters which are equally instructive and helpful. We commend the book to all who are interested in hospitals.

Studies in Cardiac Pathology. By George W. Norris, M. D., Associate in Medicine at the University of Pennsylvania, etc. Illustrated. Price $5.00. (*Philadelphia and London: W. B. Saunders & Co., 1911.*)

The stimulus for this book seems to have been the opportunity of photographing cardiac lesions. There are 85 full-page illustrations. Most of these are good, others, as might be expected from photographs of objects with three dimensions, are only sharp in areas and obscured elsewhere by shadows or high lights. A poor illustration like Fig. 36 of chronic adhesive pericarditis adds nothing, especially since there are other much better illustrations of analogous conditions. Fig. 42 does not convey the idea of concentric hypertrophy, and while gummata of the myocardium are rare, four separate full-page illustrations seem too many, as there are only two poor cuts of the much more important syphilitic lesion in the aorta.

The chapter including 10 page illustrations of congenital lesions (patent ductus arteriosus, foramen ovale and interventricular septa) would be entirely superfluous were it not for Fig. 84, aortic stenosis. A picture of the collateral circulation as represented by J. F. Meckel in 1827 would be of value here.

There is no definite system in the presentation of the subject and the various phases of cardiac pathology are only more or less completely illustrated. There are no microscopic illustrations.

The photographs are all accompanied by complete original pathological descriptions. This is one of the best features of the book. The accompanying text is brief and clear. The statistics too are of value. The bibliography does not attempt to be complete. The few minor errors in plate references, etc., are unimportant.

A Manual of Pathology and Morbid Anatomy. By T. Henry Green, M. D., F. R. C. P., etc. Eleventh Edition. Revised and Enlarged by W. Cecil Bosanquet, M. D., etc. Illustrated. (*Philadelphia and New York: Lea & Febiger, 1911.*)

This book was noticed by us in our issue of January, 1906, volume XVII, and what was said of it then holds true to-day. Considering its character it has had a remarkable success, and appears to be very popular, but as a scientific accurate work on pathology it cannot be recommended.

Immune Sera. A Concise Exposition of the Main Facts and Theories of Infection and Immunity. By Dr. Charles Frederick Bolduan. Fourth Edition. Rewritten and Enlarged. (*New York: John Wiley & Sons, 1911.*)

This is a small but first-class manual and we are glad to note its fresh appearance. Its excellent characteristics were noticed in this journal in December, 1907, volume XVIII.

A Manual of Clinical Diagnosis By Means of Laboratory Methods for Students, Hospital Physicians, and Practitioners. By Charles E. Simon, M. D., etc. Seventh Edition. Enlarged and Thoroughly Revised. Illustrated. $5.00. (*Philadelphia and New York: Lea & Febiger, 1911.*)

This work has won merited esteem and each edition is an improvement on the preceding one. The character of the work was commended in the Bulletin in February, 1908, volume XIX.

Laboratory Studies in Tropical Medicine. By C. W. Daniels, M. B. (Camb.), M. R. C. P. (Lond.), etc., and H. B. Newham, M. R. C. S. (Eng.), etc. Third Edition. Thoroughly Revised. Illustrated. $4.00. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

It would be well for all doctors going to the tropics or making a study of tropical diseases to have this book on their shelves. The authors discuss in a clear and concise way the blood and its parasites of one sort and another, insects, diptera, mosquitoes, fleas, lice, bed-bugs, arachnoidea, etc., parasites in the tissues and intestines, faeces, urine, etc. These "Studies" will prove a most helpful guide for they are well written and reliable.

A Manual of Practical Hygiene for Students, Physicians and Health Officers. By Charles Harrington, M. D. Fourth Edition. Revised and Enlarged by Mark Wyman Richardson, M. D. Illustrated. $4.50. (*Philadelphia and New York: Lea & Febiger, 1911.*)

It is to be regretted that Dr. Harrington did not live to see this new edition of his admirable work, and to continue the excellent work he was doing. Dr. Richardson is to be congratulated on his share of this new edition. The book remains, as it was before he took hold of it, one of the very best manuals on the subject

in English, and students could not have a better guide in their study of hygiene. The Manual was praised in the Bulletin in February, 1906, volume XVII.

A Manual of Surgery for Students and Physicians. By Francis T. Stewart, M. D. Second Edition. Illustrated. $4.00. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

The manuals on surgery are innumerable, and this work has no special characteristic to save it from the oblivion which is sure to fall on all but one or two within a comparatively short time. It can be recommended as a safe guide, but a student who means to make surgery his specialty will want a larger and better book than this to start out with.

Isthmian Canal Commission. A Report on Hemoglobinuric Fever in the Canal Zone. A Study of its Etiology and Treatment. By W. E. Deeks, M. D., and W. M. James, M. D. (*Published by the Department of Sanitation, I. C. C. Press, Quartermaster's Department, Mount Hope, C. Z., 1911.*)

This most interesting report should have a wide circulation, for the question of the etiology of hemoglobinuric fever has ever been one of great interest to all true students of medicine. We are especially glad to call attention to it as another bit of proof of the excellent work being done by the doctors on the Panama Canal under the able direction of Col. W. C. Gorgas.

A Cross-Section Anatomy. By Albert C. Eycleshymer, M. D., etc., and Daniel M. Schoemaker, M. D., etc. $20.00. (*New York and London: D. Appleton and Company, 1911.*)

This work is as much a credit to the publishers as to the authors, but its price will unfortunately prevent its being as much used by students as is to be desired. Its title indicates exactly the scope of the work. There are 113 plates of section drawings followed by a chapter on the "Topography of Organs," a "Bibliography" and "Index." All names are given as in the B N A. The drawings are four-fifths natural size, and on the opposite page is the explanatory text. In the introduction, which gives an interesting account of the historical development of such an anatomy as this one, the reader will also find all the detail necessary for him to have a clear understanding of these section drawings, which in this quarto edition are so large as to be easily studied. A word of commendation may be added in praise of the type which is clear and of good size.

Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. New Series, No. 45. Epidemic Dropsy in Calcutta. By Major E. D. W. Greig, M. D., etc. 2/. (*Calcutta: Superintendent Government Printing, India, 1911.*)

"Epidemic Dropsy" is merely another name for beriberi, and the main interest of this paper lies in the fact that it is the first report on the disease as seen in Calcutta. Major Greig carried on his investigations with care and skill, and his study is a valuable contribution to the already large literature on this subject.

Nervous and Mental Disease Monograph. Series No. 8. Mental Mechanisms. By Wiliam A. White, M. D., etc. $2.00. (*New York: The Journal of Nervous and Mental Disease Publishing Company, 1911.*)

The first monograph of this series by Dr. White was a most excellent one, but as high praise cannot be accorded to this piece of work. After careful reading it leaves the impression of lack of unity, as though the chapters had been delivered as lectures on one or another occasion, and then thrown together into a volume hastily, making an inharmonious whole. There is some unnecessary repetition—cf. the dreams related on pp. 28 and 37. In spite of its imperfections this monograph should prove essentially useful to students, for the author's style is simple and clear, somewhat rare qualities among the writers on psychological subjects, who mystify the reader by their maze of words, and leave him wondering as to the real clearness of the author's mind. "Mental Mechanisms" is divided into the following eight chapters, which are preceded by a brief preface and introduction: Chap. I. Some Considerations on the Constitution of Consciousness.—Relation of Mental and Physical. Chap. II. Types of Reaction.—Defense and Compensation. Chap. III. The Content of Consciousness.—Dreams.—Symbolism.—The Psychoses.—Folk-Lore. Chap. IV. Types of Complex Reactions.—Modes of Expression.—General Considerations. Chap. V. Current Conceptions of Hysteria.—Psychological, Physiological, Biological and Clinical Theories. Chap. VI. The Psychological Approach to the Problem of Art. Chap. VII. The Theory, Methods, and Psychotherapeutic Value of Psychoanalysis. Chap. VIII. Preventive Principles in the Field of Mental Medicine.

All the chapters are by no means of equal merit, perhaps due in a measure to the limit of size of the monograph, but as this is a work more fitted to the student than the advanced worker, the former can perhaps gain a better foundation as to the working of the mind from the conciseness of the manual than if it were longer.

Progressive Medicine. Vol. III, Sept. 1911. (*Philadelphia and New York: Lea & Febiger, 1911.*)

The general reviews, prepared with their usual skill by the editors, in this volume cover "Diseases of the Thorax and its Viscera, Including the Heart, Lungs and Blood Vessels," "Dermatology and Syphilis," "Obstetrics," and "Diseases of the Nervous System." The report on the use of Salvarsan or "606" should be carefully read by all who have not had a chance to inform themselves thoroughly both as to the advantages and dangers of this powerful remedy.

The Human Atmosphere or The Aura made Visible by Chemical Screens. By Walter J. Kilner, B. A., M. B. (Cantab.), etc. Illustrated. (*New York: Rebman Company.*)

The author believes he has discovered a new physical phenomenon and that all beings (human) have aura; that these aura change under varying conditions and that diseases can be diagnosed from the changes occuring in the aura. As the aura can only be seen under special conditions, and even then not without some strain and danger to the eyes, the author does not succeed in convincing us of having made a real discovery, and of not being self-deceived. It will require much longer and profounder investigation into the subject before the truth and value, if true, of this discovery(?) can be affirmed.

Oxford Medical Publications. The Sensibility of the Alimentary Canal. By Arthur F. Hertz, M. A., M. D. (Oxon.), F. R. C. P. (*London: Henry Frowde and Hodder & Stoughton, 1911.*)

In a small, nicely printed, and neat-looking volume, Dr. Hertz has reprinted the lectures he delivered this year under the Goulstonian Foundation at the Royal College of Physicians. He treats the subject in an interesting way, and his results are based in large measure on his own experiments. The final word has not yet been spoken, however, and Dr. Hertz leaves some points in rather a cloudy condition. He states that "the mucous membrane of the œsophagus is sensitive to thermal stimulation, but that of the stomach and intestines is insensitive," and in the next paragraph that "contact of alcohol with the mucous membrane of all parts of the alimentary canal gives rise to a sen-

sation of heat." The difference between this sensation of heat, and the lack of sensitiveness of the stomach to thermal stimulation is not sufficiently explained.

An Introduction to Therapeutic Inoculation. By Dr. W. Carmalt Jones, M. D. (Oxon.). $1.25. (*London: Macmillan & Co., Ltd., 1911.*)

This little book of one hundred and sixty-five pages is divided into two parts and an appendix. According to the preface, the first part is "an attempt to state in the simplest possible terms, the common sense of Therapeutic Inoculation, the object of which is to induce immunity to bacterial infection. The second part deals with the practical application of the principles" stated.

The book is characterized by inaccurate statements, extravagant claims and gross insufficiencies. For example, on page seventeen the statement is made that "Typhoid Fever, Cholera and Plague are the only diseases against which prophylactic inoculation is used to any extent at the present time." No mention is made of vaccination against smallpox except under the historical section, fifty-seven pages further on. Again on page thirty-one, the dogmatic assertion is made that "all infections due to organisms of these types (pathogenic) are amenable to treatment by vaccines." The fact that in many bacterial diseases such as typhoid fever, pneumonia, etc., the results are at best uncertain, and that in infectious endocarditis vaccine therapy may prove most harmful, finds no mention.

The classification of bacteria on page thirty-two is to say the least naïve; the description of making blood cultures is primitive and faulty; and the diagnosis of the specific infecting organism from clinical sizes alone, recommended in Chapter III, need only be mentioned to be condemned.

In the description of the technique of agglutination tests, no mention is made that the serum must be diluted. On page fifty, we find that "the opsonic index . . . . is by far the best method which is at present available for the serum diagnosis of the majority of bacterial diseases!"

The chapter on the history of therapeutic inoculation is perhaps the best one in the book though it contains not a single reference to Ehrlich and his work.

Part II, devoted to the practice of vaccine therapy is more satisfactory than Part I, but here, too, broad generalizations are drawn from meager data and though we are told in the preface that "only those infections of which there has been large experience are considered," we find statistics of the effect of vaccines in a small series of cases of whooping cough!

In the appendix there are good, though general descriptions of laboratory methods and on the preparation of vaccines.

Throughout the book, errors of rhetoric and a careless use of grammar abound. Though it contains good material the book is too elementary for students and too inaccurate to be of any great utility to anyone.

Vaginal Celiotomy. By S. Wyllis Bandler, M. D., Adjunct Professor of Diseases of Women, New York Post-Graduate Medical School and Hospital. $5.00. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

This work supplies most acceptably a need that has long been felt in the gynecological literature of this country. The author has wisely avoided extravagant claims for vaginal celiotomy as compared with the abdominal route, and, on the whole, has shown good judgment in the selection of operations for which it undoubtedly possesses distinct advantages. The illustrations are exceptionally good; and while there is an unnecessary repetition in the portrayal of certain operative steps, this is offset by the obvious advantage to the student of having each operation fully and clearly presented without the inconvenience of having to refer to other sections. The text is not intended as an exhaustive treatise, but emphasizes the essentials in a very forceful and suggestive style. If any criticism is to be made of the book, it should be in the form of a warning to the beginner that the difficulties attending vaginal celiotomy in a large percentage of cases are far greater than one would suppose from a review of this volume. Nevertheless, the work deserves the hearty endorsement of the profession, and will undoubtedly aid very materially in bringing into general favor procedures the value of which has already remained far too long unrecognized by the mass of gynecologists in this country.

E. H. R.

Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India.

No. 46 (New Series). Malaria in the Punjab. By Major S. R. Christophers, M. B., etc. Price 3/.

No. 47 (New Series). Dysentery and Liver Abscess in Bombay. Being the Report of an Enquiry carried out by Major E. D. W. Greig, M. D., etc., and Captain R. T. Wells, M. B., etc. Price 3/. (*Calcutta: Superintendent Government Printing, India, 1911.*)

Without access to these reports which are "issued under the authority of the Government of India by the Sanitary Commissioner with the Government of India, Simla, no student of these diseases can feel himself fully master of his subject. Both diseases are very prevalent in India, and there seem to be certain local conditions in the Punjab which make epidemic or autumnal malaria in that country extremely fatal and especially so to children and babies. Happily in America there is no place where such devastating epidemics occur. Even yellow fever at its worst in Cuba can hardly have been so fatal as the autumnal malaria appears to be regularly in the Punjab. Major Christopher's report will only be read by a few specialists probably but they will find it eminently worth careful study.

The report of the two officers Greig and Wells will interest a larger body of physicians for amoebic dysentery is a commoner disease than is generally supposed in this country, and this careful study will help any student in the study of an obscure case of dysentery.

The Mechanism of Life. By Dr. Stéphane Leduc. Translated by W. Deane Butcher. Price $2.00. (*New York: Rebman Company, 1911.*)

This is a work which all students of biology will be glad to have a chance to read, but it is only the specialist who can judge of the correctness of the author's views and facts. In 1907 the Academy of Sciences in Paris declined to publish a report of these experiments because the author appeared to be tending toward "spontaneous generation" as the basis of his psycho-chemical theory of life. The table of contents will indicate the difficulty of the solution of the problem of the mechanism of life, and the brevity of the work will weigh somewhat against its value in view of the different questions which have first to be solved. The chapters are headed as follows: (1) Life and Living Beings; (2) Solutions; (3) Electrolytic Solutions; (4) Colloids; (5) Diffusion and Osmosis; (6) Periodicity; (7) Cohesion and Crystallization; (8) Karyokinesis; (9) Energetics; (10) Synthetic Biology; (11) Osmotic Growth: A Study in Morphogenesis; (12) The Phenomena of Life and Osmotic Productions: A Study in Physiogenesis; and (13) Evolution and Spontaneous Generation.

Principles of Anatomy. The Abdomen Proper Described and Illustrated by Text and Plates by Wm. Cuthbert Morton, M. A., M. D. (Edin.). Price $12.00. (*New York: Rebman Company, 1911.*)

The cost of this work will limit its use greatly among medical students, and the difficulty of the combined use of the plates and text will not render it popular. It will have also to contend with

the well earned popularity of Gray and other first-class anatomies. Thus handicapped it will have difficulty in making its way, but the students who will work through it plate by plate and layer by layer will undoubtedly know the anatomy of the abdomen thoroughly, though this knowledge, tough as it is, can we believe be more readily and better acquired elsewhere and by other methods.

What to Eat and Why. By G. Carroll Smith, M. D. $2.50. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

The value of this work rests largely in its simplicity, and yet, so far as the author goes, thoroughness. It is a good book for students and for the laity—though where regular diets have to be prescribed it is far better for the patient to take the advice of a physician than to follow any book absolutely. The author begins with an introductory chapter on foods and digestion, and then in the succeeding chapters takes up special diseases and explains in a rational manner the diets best suited to each. There are many more extensive and pretentious works on this same subject, but this one will serve its readers as a safe guide.

Cesare Lombroso. A Modern Man of Science. By Hans Kurella, M. D. Translated from the German by M. Eden Paul, M. D. (*New York: Rebman Company, 1911.*)

Dr. Kurella's study of Lombroso and his work is both interesting and sympathetic. To those unable to read Italian this brief sketch of a great man will be welcome. How great the man was is known to but a few, for most associate his name alone with his work on marks of degeneracy in the human race and their association with crime, and the majority of readers have a very false idea of what Lombroso's final ideas about this relation was. Few recognize that he was the first to study pellagra thoroughly, and that he was hounded by the profession for the utterance of his views as to its cause, and driven from Pavia where he was practising. To-day his intoxication theory is the one most generally accepted by the leading authorities on this disease. Lombroso did not give in to the attacks upon him, but quietly pursued his way and before he died the merit of his work happily was known. But in the study of criminal anthropology and psychology, wrong as some of his views may be, he will always have to be recognized as a leader, for his work was most thorough and exhaustive and it is due to him that criminology has become such an important study to-day in the solution of questions connected with social economy and welfare. The criminal owes much of his better treatment to Lombroso's teachings. Towards the end of his life he turned to the study of spiritualism and believed in it; his own attitude is well worth quoting: "Every epoch is unripe for the discoveries which have had few precursors; and if it is unripe it is also unadapted to perceive its own incapacity. The repetition of the same discovery prepares the brain to make it its own, to accept it, and finds minds gradually becoming less hostile to its acceptance. For nearly twenty years the discovery of the cause of pellagra was regarded throughout Italy as mad; to-day the academic world still laughs at criminal anthropology, at hypnotism, at homeopathy. Who knows whether we, who to-day laugh at spiritualism, may not also be in error? Thanks to the misoneism which is concealed in us, we are, as it were, hypnotized against the new ideas, incapable of understanding that we are in error, and like many insane persons, whilst the darkness hides the truth from us, we laugh at those who stand in the light." Although this was written in 1883, it explains clearly his later activities in regard to spiritualism, and shows his open-mindedness and breadth of view. Kurella, who is an ardent admirer of his teacher and friend, ends this life with a singularly unfortunate phrase. Speaking of Lombroso's last work on hypnotism and spiritualism he says: "We, however, who renounce the 'Spirit-World,' may well content ourselves with the undying intellectual achievements of the deceased investigator; to our enemies we freely give the Lombroso of *senile decay* [the *italics* are ours], for the Lombroso of youth, forever young, is ours." The phrase *italicized* is unkind to say the least, for there are many who believe in the "Spirit-World," who give no sign of senile decay, and it seems to us that Lombroso's attitude as evidenced in his own words quoted above should have kept the author from such a sneer. Otherwise there is no fault to be found with the book, the translation is smooth, and it is fortunate that such a clear exposition of Lombroso's work should be attainable by all occupied in the study of criminology.

A Pocket Medical Dictionary. By George M. Gould, A. M., M. D., etc. Sixth Edition. Revised and Enlarged. $1.00. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

Dr. Gould's reputation as a lexicographer has long been well established and all his dictionaries are books of distinguished merit. There is no doubt that this is the best pocket medical dictionary in English. The new edition contains 34,000 words, is readily portable, the type is clear, and its price brings it within the reach of all students. It is a most useful book for any physician to have close at hand.

Surgical Applied Anatomy. By Sir Frederick Treves, Bart., etc. Sixth Edition. Revised by Arthur Keith, M. D., etc. Illustrated. (*Philadelphia and New York: Lea & Febiger, 1911.*)

This has long been a deservedly popular work with students, and will, there is little doubt, long remain so. The common power of the great English clinicians, so rare among most medical writers, of presenting their subject in an attractive and interesting way is one of the author's gifts and explains in part the merited success of this book. Those who have used it know its many excellencies. "The alterations in the new edition relate to glands of internal secretion, to the lymphatic system, to the anatomy of the abdomen, and to new facts which have been discovered by the use of X-rays in examining the human body," but in size and form and color this old favorite remains unchanged.

International Clinics. Vol. III. 21 Series. $2.00. (*Philadelphia and London: J. B. Lippincott Company, 1911.*)

The usual variety of clinical articles on various diseases and conditions with certain general papers dealing with the broader aspects of the practice of medicine are to be found in this volume. The distinctive quality of the "International Clinics" is the method of handling the subjects under consideration—each writer treats his problem from a practical standpoint, and it is this feature which has helped to make the series so popular, as well as the excellent selection of authors and topics.

Handbook of Suggestive Therapeutics, Applied Hypnotism, Psychic Science. A Manual of Practical Psychotherapy, Designed Especially for the General Practitioner of Medicine and Surgery. By Henry S. Munro, M. D. Third Edition. Revised and Enlarged. $4.00. (*St. Louis: C. V. Mosby Company, 1911.*)

Any medical book which has achieved a third edition must have filled a want and be deservedly popular. The author has very successfully stated facts in a simple way, which are ordinarily couched in technical language, and has added many illustrative cases to render things still more clear. He deserves great credit for his work and we believe that every practitioner, who is not already familiar with the cardinal principles of psychotherapy, will gain much by a perusal of this work. Sound common sense is the keynote of the whole work. W. R. D.

Fiske Fund Prize Dissertation. Vaccine-Therapy. By WILLIAM C. DWINELL, M. D. (*Providence: Snow & Farnham Company, 1911.*)

The author, who is an advocate of this method of treatment for a variety of diseases, has written a brief but clear review of the status of vaccine-therapy to-day. It will be useful to the general practitioner by giving him an idea of what can be done with vaccine. Their value is still *sub judice*, but there is little doubt that they are efficient in some instances.

Refraction and Visual Acuity. By KENNETH SCOTT, M. D., etc. Illustrated. $1.75. (*New York: Rebman Company, 1911.*)

This book will serve to impress on the reader the fundamental points to which his attention will be called in the early days of his practical work in the eye clinic; but as the subjects are covered in a very superficial way the real value of the book is small. Its importance to American readers is still further lessened, as in our clinics the plane mirror is mostly used in skiascopy and a different position on the trial frame of the degrees is in vogue. Considerable space is given to the insertion of special tables of the visual requirements of the various services and railroads. As one interested depends only on the very latest printed and authorized instructions, which are subject to modifications and changes at any time, it would seem that the insertion of these tables was superfluous. Instead, one model table would better serve the needs of the general reader. This book at its best gives only a superficial description of elementary optical principals, found for the most part in the ordinary text-books on the eye, and hence its field for usefulness is limited. The topography of the book is not especially pleasing to the eye, and the author is not as careful in his choice of words as should be reasonably expected from him, in a book of this class.

B. B. B., Jr.

Manual of the Diseases of the Eye for Students and General Practitioners. By CHARLES H. MAY, M. D., etc. Seventh Edition. Revised. Illustrated. $2.00. (*New York: William Wood and Company, 1911.*)

We are glad to see another edition of May's unpretentious, yet so thoroughly satisfactory text-book on the eye. The subject matter is thoroughly modern, well balanced, and skilfully arranged. The author gets right to the point of a description of the diseases and their treatment, and but little space is given to theoretical, and controversial matters, which is in part responsible for its popularity with medical students, who can, necessarily, devote but a short space of time to the subject of eye diseases. Again, the fact that it has now appeared in six foreign languages is more than sufficient commendation for its merits. A thoroughly satisfactory index still further enhances its real worth.

If more text-book makers would examine "May" carefully before putting their own productions on the market, we should not have occasion to so often call attention to the uselessness of most of the small books on the eye, which appear from time to time, and which fall far short in merit to this excellent text-book.

B. B. B., Jr.

An International System of Opthalmic Practice. Edited by WALTER L. PYLE, M. D. *Pathology and Bacteriology.* By E. TREACHER COLLINS, F. R. C. S., and M. STEPHEN MAYOU, F. R. C. S. Illustrated. $4.00. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

Numerous articles describing the pathological changes, occurring in diseased or mal-formed eyes, especially the microscopical appearances noted, have appeared in various journals in the past few years, but these detailed descriptions are usually not given in the ordinary text-book on eye diseases, and the present book supplies a need in a satisfactory manner. While one acquainted with pathology can usually visualize just what the changes would be, yet the specific description of actual cases is more positive and convincing and this book is full of such material. It is descriptive in character, and not much attention is given to the causes that have inaugurated the pathological changes; and had more of the experimental work, which has been done in connection with animals' eyes been included, it would have been considerably more interesting and stimulating. It, however, limits itself more especially to the pathological findings in actual clinical cases.

Little attention has been given by the authors to the consideration of such problems as the passage of fluids to the interior of the eye, or to the still obscure subjects of sympathetic ophthalmitis and the etiology of cataracts. On the whole, the authors give a very correct account of the clinical and microscopical pathology of the diseases of the eye, and the work can be commended to the general reader, but it certainly cannot be considered, in its present form, as a book giving an exhaustive account, or the final word on the pathological problems pertaining to the eye. The most satisfactory reading matter is found in connection with the material devoted to the diseases of the uveal tract.

B. B. B., Jr.

Lippincott's New Medical Dictionary. Edited by HENRY W. CATTELL, M. D. Illustrated. Second Edition. $5.00. (*Philadelphia and London: J. B. Lippincott Company, 1911.*)

The first edition of this work appeared only a little over a year ago; that a new enlarged edition should be called for within so short a time is itself proof of the success of this dictionary, gratifying evidence that the profession have appreciated its merits. Medicine is such a broad subject—including so many sciences, such as chemistry, physics, biology, etc., which formerly had but slight connection with it—that a medical dictionary must include many words which seem to have but a distant connection with medicine, and there is a danger that medical dictionaries will lose their character and be overburdened by the new words which are constantly being added to the allied sciences. It is difficult to know where to draw the line, for many persons are not able to buy more than one or possibly two dictionaries, and so for them the larger and more comprehensive works are, within certain limits, the best; but there seems to be a growing tendency to include chemical terms in large numbers and this we believe to be a distinct mistake.

Another error we believe exists in defining all possible words with a common prefix, like "pseudo," "hyper" and "poly"—an intelligent person does not need such help and dictionaries might be shortened by the omission of many words with this and similar prefixes. There are many other needless definitions; take, for example, but one that we chanced upon in this dictionary—"cordate—shaped like a heart." Then follows immediately "C . . leaf —a heart-shaped leaf." This seems absolutely unnecessary; what else could it be? Other apparently needless definitions are to be found under the word "dilatation." If erroneous spelling of words are admitted there can be no limit to the size of a dictionary, example "Paramœcium, an erroneous spelling of "Paramecium." Could not such a list be added to indefinitely?

Illustrations in this, as in all illustrated medical dictionaries, have little to be said for them—they are invariably, one may say, poor, and there seems to be no system used in their selection. But it is not intended to pick flaws in this dictionary; it is an excellent one and to be heartily endorsed. Others also exist which can be warmly praised, some larger and some smaller, so that when it comes to selecting "one" the choice is difficult, but none will go astray who purchases Dr. Cattell's by preference.

Food Values Practical Tables for Use in Private Practice and Public Institutions. By Edwin A. Locke, M. D. $1.25. (*New York and London: D. Appleton and Company, 1911.*)

This is an excellent manual not only for students of medicine, but for practitioners and nurses. To the latter it ought to be invaluable. Dr. Locke deserves much praise for the admirable way in which he has arranged his tables, and his introduction, brief as it is, is clear and wise. He is not a faddist like so many experts on nutrition and diets. He presents some of the general principles of dietetics in an easily comprehensible manner in his introduction and after reading this the use of the tables is made easy for any intelligent person. The success of this work is assured for there is no other of the kind which is so practicable and so well prepared.

Pathological Technic. Including Directions for the Performance of Autopsies and for Clinical Diagnosis by Laboratory Methods. By F. B. Mallory, M. D., Associate Professor of Pathology, Harvard Medical School; and J. H. Wright, M. D., Director of the Pathological Laboratory, Massachusetts General Hospital. Fifth Revised Edition. Illustrated. 1911. $3.00.

Dorland's American Illustrated Medical Dictionary. Sixth Revised Edition. 1911. $4.50.

The Treatment of Fractures: With Notes upon a Few Common Dislocations. By Chas. L. Scudder, M. D., Surgeon to the Massachusetts General Hospital. Seventh Edition. Revised and Enlarged. Illustrated. 1911. $6.00.

A Text-book of the Practice of Medicine. By James M. Anders, M. D., Ph. D., LL. D., Professor of the Theory and Practice of Medicine and of Clinical Medicine, Medico-Chirurgical College, Philadelphia. Tenth Revised Edition. $5.50.

A Text-Book of Physiology: for Medical Students and Physicians. By William H. Howell, Ph. D., M. D., Professor of Physiology, Johns Hopkins University, Baltimore. Fourth Edition. Revised. 1911. Cloth, $4.00. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

It is a pleasure to call attention to these five notable works, all appearing in new editions. Their success testifies to their merits, and is an indication that they have well met the demands of the profession.

The clearness, simplicity and practicality of Wright and Mallory's Pathological Technic makes it an eminently useful book to the student; there is no other book in English which covers the ground so satisfactorily.

In view of the fact that there are several other medical dictionaries—Gould's, Stedman's and Cattell's—which have their distinctions and admirers, the demand for a sixth edition of Dorland's is a sure proof that its excellencies have appealed to many doctors.

Scudder's work, admirably illustrated by X-ray and other photographs, is a classic and has been so often warmly commended that it demands no further praise.

The favorable reception of Anders' Text-Book of Medicine is noteworthy; it has been carefully revised, and new material has been added, so that the new edition will be welcomed by many.

There is no question that Howell's Text-Book of Physiology is the best in the English language, and the appearance of the fourth edition shows that its value is being more and more generally recognized by teachers and students. Since its first appearance the importance of the work has grown, and as a text-book, its merits are of the highest order.

The publishers are to be complimented on the handsome appearance of these books, and also on their activity in republishing these standard medical works.

Collected Papers by the Staff of St. Mary's Hospital (Mayo Clinic) 1910. Illustrated. $5.50 (*Philadelphia and London: W. B. Saunders Company, 1191.*)

It is but a short time ago that the first volume of papers from this staff appeared, and in this second handsomely printed volume there are a series of important articles on The Alimentary Canal, Hernia, Genito-Urinary Organs, Ductless Glands, Head, Neck, and Extremities, Technic, and General Papers. As the product of a purely surgical hospital, this a remarkable collection, and all surgeons will be anxious to own in collected form the papers by the Mayo Brothers, as they are commonly called, and their pupils and assistants.

The Practice of Medicine. By Frederic Taylor, M. D., F. R. C. P., Consulting Physician to Guy's Hospital, London. (*New York: The Macmillan Company, 1911.*)

This is one of the popular British text-books of medicine and the present is the ninth edition. The author has partially disarmed criticism of his arrangement by expecting it in his preface. We should not agree with him in placing pneumonia among the diseases of the respiratory system. He does not place typhoid fever under the digestive tract. Attention is at once drawn to the inclusion of a section on diseases of the skin. Perhaps it is an advantage for the student but on the whole we doubt the wisdom of this. The descriptions of skin diseases have to be brief and the space might better be used to allow fuller descriptions of disease generally. However, this is a matter of opinion. A satisfactory feature is a general preliminary section of each system before the special diseases are considered. In these there is some reference to diagnostic methods which is necessarily brief but much is compressed into them. For example, the main points in the physical examination of the chest are well summarized in a few pages. There are some points in terminology which deserve comment. The author uses the adjective *tubercular* to designate conditions due to the tubercle bacillus but it seems preferable (as suggested by Macalister) to use *tuberculous* for this and employ tubercular to designate morphological changes characteristic of anatomical tubercle. Thus we might speak of tubercular syphilides, tubercular leprosy, etc. The use of "phthisis" for pulmonary tuberculosis seems a step backward as no universal meaning is attached to the term. It has as many meanings as pronunciations. The relative space given to hysteria, neurasthenia and hypochondriasis is unusual. Hysteria has about ten pages—and an excellent section it is—neurasthenia less than one page and hypochondriasis a little over one. For American readers it is a surprise to find so little attention given to neurasthenia (once called the English Malady) and so relatively much to hypochondriasis. We question if many would agree with the author in the conditions which he considers under hypochondriasis. The discussion of the treatment of these disorders takes little notice of the newer psychical methods.

However, these are minor points and the work as a whole is well worthy of high commendation. There is an excellent division of space among the subjects with reference to their relative importance. The descriptions throughout are clear and reference to recent work has shown that the author has brought this edition up to date. One omission is the lack of any reference in the section on pellagra to its occurrence in the United States. Altogether it is recommended as an excellent work and a satisfactory text-book of medicine.

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BULLETIN

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JAMES PARKINSON.*

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English born and bred, an English physician and scientist, forgotten by the English and by the world at large—such is the fate of James Parkinson.

To Mary, wife of John Parkinson, a son was born on the 11th of April, 1755. On the 29th day of the same month the child was baptized and named James. These facts are recorded in St. Leonard's Shoreditch Parish Register, Middlesex. I was unable to find the date of his birth noted in any biography.

Concerning the life of John Parkinson, father of James, nothing is known. However, while searching the old Shoreditch parish churchyard last summer for the tombstone of James Parkinson, a stone was discovered, from which time has almost erased the inscription, but upon that part of the stone which is protected by an overhanging roof or sheltering hood the following can yet be readily seen:

To
the Memory of
Jno. Parkinson, Surgeon
late of this Parish
who died on the 10th
day of Jan. 1784, in
the 69th year of his age.

An inscription of twelve lines originally followed this but the passing years have so completely effaced it, that at present only an occasional letter or word can be deciphered.

This, however, is enough; and sufficient to indicate that Parkinson was born into a family of some standing and culture and that his father lived long enough to arrange for and to personally supervise his medical as well as his preliminary education.

The family lived at No. 1 Hoxton Square, in the borough of Hoxton, which at present constitutes part of the East Centre of London. Formerly, Hoxton Square, surrounded by the homes of wealthy families was a most desirable residential locality. It boasted of its residents, its homes, its carriages, its servants and of all that accompanies culture and wealth.

Hoxton Square was formerly a parish square, only the residents on the square being privileged to enjoy its attractions, each family having a key whereby admittance was gained. It was an attractive place. There still stands in this park, close to Parkinson's home, an immense and beautiful plane-tree, an Oriental ansifolia, which has attained the age of 150 years. Parkinson must have known it in his youth, it grew up with him, and he must have learned to love it. Today, however, Hoxton is a public square, open to all, not surrounded by homes of the wealthy but by all varieties of small factories

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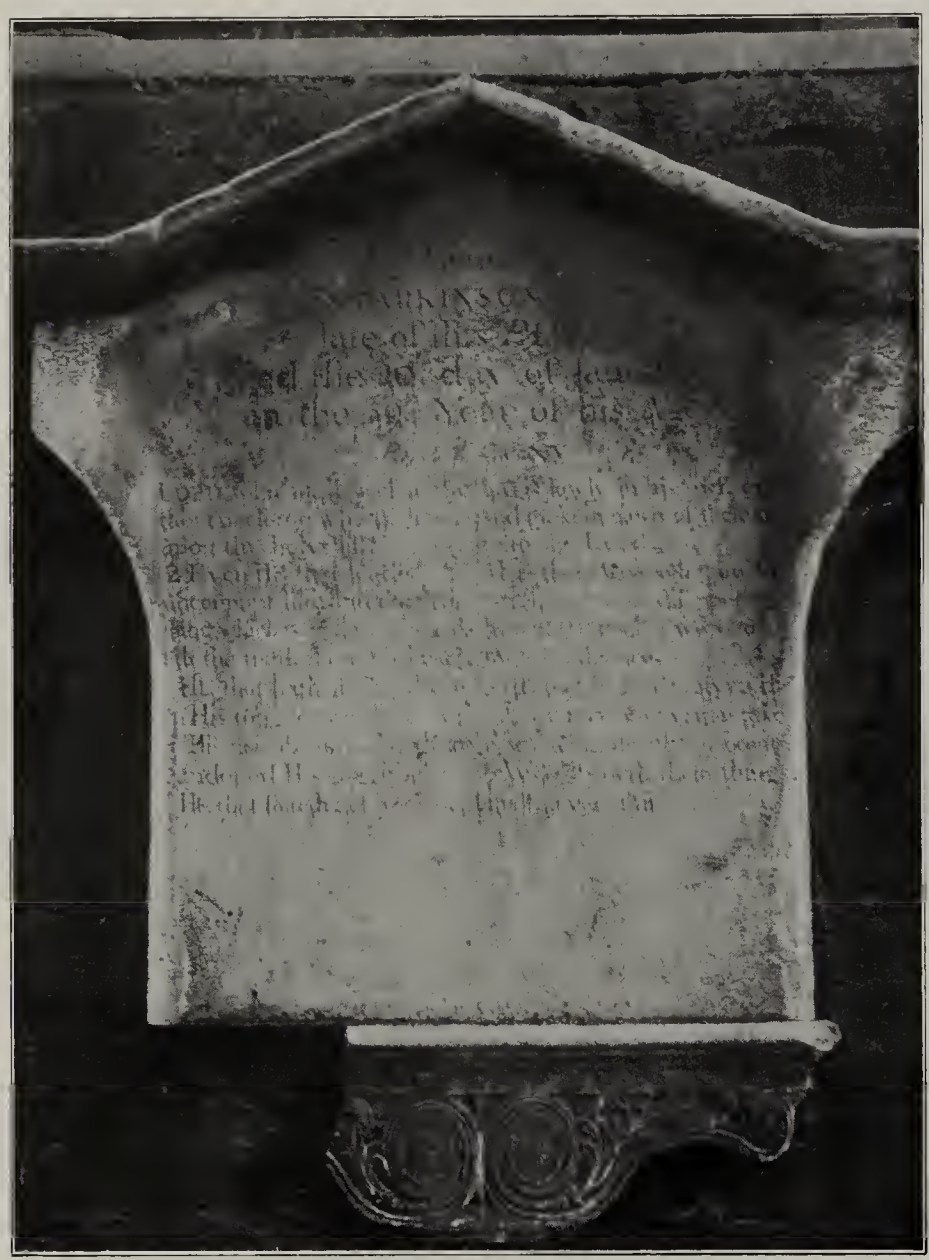
and work shops. Marble masons, mattress makers, French polishers, cabinet manufacturers, carvers and guilders, leather embossers, drafters, plate and sheet glass makers, now occupy and carry on their work in what were formerly the homes of the wealthy and influential.

The old house at No. 1 Hoxton Square still exists. From without it has partaken of the fate that has befallen the neighborhood and suggests only age, neglect, poverty and even squalor, but from within it recalls days of prosperity, of culture and even of luxury.



Tombstone of John Parkinson.

The house is a plain old three story building facing the east, on the northwest corner of Hoxton Square. Behind the main building and connected with it is a smaller two-story one with a central door opening into the little side street. This apparently was Parkinson's office. Behind this again is another smaller building which may have served as a laboratory, as a library, or perhaps as a museum. Leading up to the deeply set, black, massive looking front door are a stone walk and deeply worn stone steps. The house is only a few feet back from the street and before it stands an old iron fence.

Uninteresting though the exterior is, upon entering this building one is impressed at the large size of the rooms and with the evidences of the prosperity of other days. We see in almost every room great carved open fire-places of elaborate design, and between some rooms large connecting arches. The deep panelling of walls and ceiling which was formerly so much in vogue is well preserved in some of the rooms on the second floor. One is surprised to find such an interesting interior behind such an uninviting exterior.

Parkinson, then, was brought up in a medical atmosphere in the midst of pleasant surroundings, inheriting his father's tastes and in all likelihood his practice, for we are informed that he, James, was already in active practice in 1785 during which year he attended Hunter's course of lectures on surgery. His father's death occurring in 1784 makes it more than probable that the practice passed from the father to the son. This probability is increased from the fact that his entire life

No. 1 Hoxton Square.

was spent in the same neighborhood, all of his books being dated from Hoxton Square and his death occurring in Kingsland Road, but a few hundred yards from Hoxton Square.

Concerning his medical education we know little, but from a perusal of his little book entitled "The Hospital Pupil" much can be inferred both as to his preliminary and as to his medical education. The title page reads:

The Hospital Pupil

or

Observations addressed to the parents of youths intended for the profession of medicine or surgery on their previous education, pecuniary resources and on the order of their professional studies with *Hints to the young pupil* on the prosecution of hospi-

tal studies, on entering into practice and on medical jurisprudence. (Written in reply to an appeal for advice from a friend educating a son.) 1800.

Parkinson here insists on the necessity of a suitable temperament and a correct attitude of the student towards the study of medicine.

After the common school education the student should possess a knowledge of Latin and of natural philosophy. As he says:

The grand object which next calls for consideration is what is the best situation in which a youth can be placed and what is the mode of study, which will most certainly secure him all the theoretical and practical knowledge, in the science of healing, which, may be obtained under the excellent arrangement for professional studies, with which the metropolis abounds.

According to the present system, the first care of the parent who has a son whom he intends shall be educated in both branches of the healing art, is to find out some gentleman of respectability who is properly established as a surgeon and apothecary. With him, paying a proper premium, he fixes his son, who has received a common school education, as an apprentice for seven years. At the end of this period he is in general, sent to one of the hospitals in the metropolis, where he attends the lectures, and witnesses the practice of the hospital for a twelvemonth or even less time, and, then if a favorable opportunity offers, takes charge of the health of some populous neighborhood.

Now, on full conviction, I assert, that of all the modes which could be devised for a medical and chirurgical education, this is the most absurd: and is the one which would most certainly exclude a young man from the chance of acquiring that knowledge, which the important situation he is about to fill, so imperiously demands.

When I consider that this has been the plan of education adopted for many of those gentlemen who with so much credit to themselves and advantage to their employers, practice both branches of the profession, in every part of the country, and that it is the mode of education which is almost universally adopted, I can not but be thoroughly aware of the consequences of the assertion that I make. It is indeed much more calculated to provoke contradiction than to obtain assent. This consideration does not, however, prevent its being hazarded, nor should it, since the opposition, I expect it may experience, will point out the great number of those who think differently from me, and who require, I venture to believe, to be freed from the delusions of a mischievous error.

The first four or five years are almost entirely appropriated to the compounding of medicines, the art of which with every habit of necessary exactness, might be just as well obtained in as many months. The remaining years of his apprenticeship bring with them the acquisition of the art of bleeding, of dressing a blister and for the completion of the climax—of exhibiting an enema.

Many young men with their minds thus sparingly cultivated are sent to the hospitals in the metropolis where in consequence of the previous mismanagement of their education, the plan of instruction, otherwise so well contrived loses all its advantages and appears with respect to such students to be fraught with equal absurdity with that which preceded it.

When the student is limited to a short term of hospital practice and does not possess extraordinary abilities and industries, the whole of that period on which his future prosperity and his ease of conscience must depend may slide away only furnishing him with a knowledge of the multiplicity of subjects of which though he is convinced they are absolutely necessary to be known, he finds himself miserably ignorant.

He then discusses the need of a preliminary training either in a university or under a private tutor and insists on the need of Latin, Greek and shorthand. In the medical course he advises: during the first year—Attendance at a course of anatomical lectures together with some knowledge of the several branches of natural philosophy; in summer read anatomy and physiology in Latin, chemistry, physics, French and German. 2d year: Anatomical lectures, physiology, practical anatomy; in summer read Haller, Monroe, Blumenbach, Bichat and Cullen, also some chemistry, natural philosophy, surgery and materia medica. 3d year: Attend clinical lectures. 4th year: Morbid anatomy, clinical work. 5th year summer: Serve as a dressing pupil, see clinical work and attend lectures. He concludes "Thus with no more expense, four or five years advance in knowledge would be obtained, the advantage of which through life must be immeasurable. In a word, I am confident that for a young man intending to practice both professions, no apprenticeship will be advisable except to a hospital, and that the advantages of attaching him to a hospital in the manner I have proposed are incalculable."

The second part of the book consists of advice and a plan of study in order that as much advance as possible can be made within the small space of twelve months.

A footnote on page 144 embodies the ideals of the council on pharmacy:

In this age of science and beneficence, it is surprising that no public-spirited and wealthy men have stepped forward to form an association and establish a fund for the purpose of ascertaining the actual properties of every nostrum, of promoting the recompense of any one who published any useful discoveries in medicine, and of furnishing with counsel, and, the means of prosecution, those whose healths have been injured and whose properties have been stolen by ignorant pretenders to medicine, whether under the characters of advertising quacks, cancer curers or regulars.

The tone of this book suggests that Parkinson was speaking of the advantages of the hospital apprenticeship from his own personal experience and his other various publications lead one to infer that he had also had the preliminary education here advised.

When twenty-six years of age he married Mary Dale in St. Leonard's Shoreditch Church on May 21, 1781. On February 11, 1783, a son, James J., was born. A second son, John William Keys Parkinson, was born on July 11, 1785. He grew up, was educated for and practiced medicine, becoming in 1834 a fellow of the Royal College of Physicians. After his father's death he continued the practice at No. 1 Hoxton Square and in 1833 published a book entitled "Hunterian Reminiscences," which was really Hunter's course of lectures on surgery which had been taken down verbatim in shorthand by his father in 1785 and later transcribed. As to the other children we learn from consulting his will that James Parkinson had at least one other son and two daughters.

The name Keys, given his son in 1783, considered in con-

nection with his will written forty years later, in which John Keys is named as an executor and as a beneficiary shows plainly that Parkinson enjoyed with Keys a long and deep friendship which lasted from his early life until his old age. In Mr. Parkinson's examination before the Privy Council[1] he was questioned concerning a certain Mr. Keys, a counsellor, without doubt the same Keys. The fact that in the will Parkinson's sister is called Mary Keys would suggest that Keys had married Parkinson's sister. Be that as it may, Parkinson enjoyed one of the greatest assets in life—a true life-long friend, concerning whom I have been unfortunately unable to discover any further particulars.

The wide-spread nature of Parkinson's interest in life was early manifested in his great activity in various directions. His clinical work did not deter him from entering other fields of thought and learning, and wherever he entered his attitude was that of fearlessness and confidence. He always attacked that which appeared wrong to him regardless of what and of whom it involved.

He partook of the spirit of the troublesome times in which he lived. He was a reformer, a radical. Born during the progress of the seven years' war, he lived during the most restless period in modern history. He saw the American fight for independence and witnessed the formation of the great new republic. He lived through the period when France was in the grip of the revolutionists, through the reign of terror, the days of Marat, Charlotte Corday, Marie Antoinette, Danton and Robespierre—days of the guillotine. He saw Napoleon carry war into every land and he probably celebrated in the great rejoicings following Trafalgar and Waterloo.

He linked arms with other reformers although the nature of the times made such action dangerous. Behind closed doors he met with them, discussed and planned for the dawn of better days for England. He was a member of secret societies whom the government feared and constantly watched. He was not content with planning but wrote on reform, his writings being eagerly read by thousands of dissatisfied spirits who though recognizing that conditions were not right, did not know who was to blame or how redress could be obtained.

In 1794 he wrote a pamphlet entitled "Revolutions without Bloodshed; or Reformation Preferable to Revolt." He opens by saying:

It having been industriously asserted that the happiness and prosperity of the people would not be at all increased by a Reform of the Representation, it has been thought proper to publish the following enumeration of those changes which in all probability might be thereby produced.

I.

The Claims of the People might be more duly attended to and their Rights restored.

II.

Taxes might be proportioned to the abilities of those on whom they are levied, and not made to fall heavier on the poor than the rich.

III.

The present system of Excising almost all the necessaries of life, as soap, candles, starch, beer, etc., etc., might be abolished.

IV.

The Poor Laws and Laws of Settlements might be amended, and a poor man not be liable to be sent to prison for moving out of his own parish to seek employment.

V.

The Game Laws might be abolished, and the farmer be no longer obliged to permit his rich and insolent neighbor to trample his fields in pursuit of an animal, which, though fed by the produce of his own grounds, the farmer himself dares not kill, but under the penalty of fine and imprisonment

VI.

Workmen might no longer be punished with imprisonment for uniting to obtain an increase of wages, whilst their masters are allowed to conspire against them with impunity.

VIII.

Some proportion might be preserved between Crimes and Punishments and the starving purloiner of a few shillings not suffer the same punishment as a murderer.

IX.

The Clergy might be provided for by an income more regularly proportioned, and levied in a more agreeable and respectable mode. A part of the vast revenues of the Bishops might relieve our numerous starving Curates.

XIII.

Families that are comparatively starving might be exempted from contributing towards the enormous sums squandered in unmerited Salaries and Pensions

XVIII.

The blessings of Peace might not be exchanged for the miseries of War, with the wicked but vain hope of riveting chains on thirty millions of men, who had resolved to be free.

XIX.

Young men might no more be trapanned from their friends to perish in the field of infamy and murder.

XX.

Our Sailors might not be dragged like felons into a service they dislike, and made accomplices in slaughter.

XXII.

Difference of Opinion in Religious Matters might not exclude men from enjoying the same benefits with their Fellow-Citizens.

XXIV.

The Expenses of the Nation might not then exceed, as they now do, the enormous sum of 80,000 £ a day—3000 £ an hour—50 £ a minute. Etc., etc.

Among other secret societies he was a member of the London Corresponding Society. Shortly after the imprisonment of Hardy, Tooke, Thelwall, Burke, etc., several members of the London Corresponding Society were placed under arrest and charged with complicity in what was termed the Pop-gun Plot. It was charged that the members of this society had formed a plot to murder George III of England. This was to be accomplished by shooting the king, during a play in the

[1] *Vide infra.*

theatre, with a poisoned arrow discharged from a pop-gun. It was also charged that the society was importing four thousand pikes from abroad and that they intended starting a revolution. Several members were seized, thrown into prison and there detained for months without being brought to trial.

Although an active member, Parkinson was not apprehended. No sooner, however, were the arrests made than he became very active, writing a long pamphlet entitled "A Vindication of the London Corresponding Society," in which he maintained the innocence of those accused and clamored against the suspension of the Habeas Corpus Act and further detention of those imprisoned without trial. He also became interested in raising subscriptions for the wives and children of the imprisoned members of the society.

In order to assist his friends in distress Parkinson did every thing in his power to have the Privy Council take some definite action. His part in the affair is clearly stated in a long letter written to Mr. Smith, one of the imprisoned. This letter appeared in 1795 in a pamphlet entitled "Assassination of the King!" In which he shows his fearlessness, but respect for the laws; also his pity for the incarcerated, and his righteous indignation with the lack of consideration and cruelty shown them.

The first intelligence I received of your being apprehended was from the newspapers. Although I sincerely regretted the situation in which you and your fellow-sufferers were placed, I could not forbear laughing at the account of a plot said to have been formed by men, whom I knew were at enmity with each other; and which proposed the destroying of the King, in so public a place as the play-house, by an arrow, which was to be armed with a miraculous poison, and to be discharged from an air-gun, leisurely levelled for aim, in the midst of a crowded audience. I concluded such a story could not obtain a moment's credit, and expected your immediate discharge.

But when I learnt that the Privy-council were proceeding with as much solemnity in their examinations, as if their political, I mean their *official* situations, were at stake, I began to suspect they had been *alarmed* into belief of the silly tale. This suspicion was, however, soon dismissed, and the more probable conjecture forced itself on my mind—that the Ministry had seized on this absurd accusation as a fortunate circumstance, which, if properly managed, might excite a sufficient degree of *fresh* alarm, to induce the public at large, but more particularly the Grand Jury, who were then sitting in examination of the bills prepared against Messrs. Hardy, Tooke, Thelwall, etc., to believe that *Treason* was actually abroad. I endeavored in vain to chase from my mind that you and your fellow-prisoners were to be held out to the world as liable to be *hanged*, *drawn*, and *quartered*, for your *imputed* crimes, the more certainly to secure to Messrs. Hardy, Tooke, Thelwall, etc., the same punishment, for copying the best action of the whole of the political lives of those apostates, Mr. Pitt and the Duke of Richmond.

Convinced of your innocence, and willing that ministers should not have it in their power to plead ignorance, I resolved to state those circumstances which had produced that conviction, to the Privy-council. I therefore had their Lordships informed, that I was willing, even on oath, to inform them of such facts as had come to my knowledge respecting your connection with Upton, your accuser

* * * * * * * *

Immediate on being called into the Council-chamber, one of the clerks, in consequence of a sign made by Mr. Pitt, put a book into my hand; upon opening it and discovering it was the New Testament, I closed it again and laid it upon the table. Mr. Pitt rising immediately from his seat, and addressing me rather sternly, said, 'What is that for, Sir?' and to the clerk, in an imperative tone, 'Administer the oath.' But not being disposed to take the oath with so little consideration, the following dialogue took place:

P. My Lords, previous to taking an oath, I must beg to be informed on what points I am to be examined?

Mr. Pitt (*in a softened tone*). That, Mr. Parkinson, is impossible.

A. My reason for asking that request is, because if I am to be examined respecting the business of Smith, Le Maitre, Higgins, and Upton, I shall, with the utmost willingness, deliver my testimony on oath; but if my examination is to extend to any other matters, I must decline the oath.

Mr. Pitt. It is not in your power, nor is it in ours. Mr. Parkinson, to make such a distinction. You are here to answer certain questions respecting *matters of the highest importance to the state*, in which any reservation on your part will at least be highly improper.

Mr. Atty. Gen. Consider, Sir, you are now before the *highest court* in this kingdom.

A. If I thought your Lordships would confine your interrogatories to the business of the *pretended plot*, I should be ready to take the oath directly.

Mr. Pitt. Then I will tell you, Mr. Parkinson, that the business on which you were required to attend is that of Mr. Upton's; but your own good sense will tell you that in the performance of our duty, we cannot engage to confine our questions to any specific matter; since that may arise, in your answers, which may render it necessary to put such questions as may not appear to apply immediately to that business.

A. Well, my Lords, as it is on the business of Upton on which I am to be examined, I am ready to take the oath, your Lordships allowing me to object to certain questions.

Aye, aye, very well, very well, was heard from every part of the table. The Attorney General saying in a very low tone of voice, 'You will not be asked to criminate yourself.' To which I answered in the same tone, 'There is no question you can put can produce an answer to criminate me.'

The oath being administered, after some unimportant questions, Mr. Pitt asked, Do you know Smith?

A. I do.

Mr. Pitt. How long have you known him?

A. I believe about two years. I was proceeding, when Mr. Pitt said, Speak slower, Mr. Parkinson, so that the clerk may take down your words.

A. If you please, Sir. But I think I could suggest a better mode of examination to their Lordships.

Mr. Pitt. Ha! What—what is that?

A. That your Lordships will allow me to give you an uninterrupted detail of what I know, subject to your subsequent examination. I am sure it will save both your Lordships and myself much time and trouble.

Mr. Pitt. Very proper, Sir; we shall be much obliged to you.

All their Lordships assenting, I proceeded to inform them of what had come to my knowledge, in nearly these words.

* * * * * * * *

Mr. Atty. Gen. When did you see Hodgson?

A. Last night.

Q. Where did you see him?

Mr. Pitt. What do you mean, Sir, you must answer the question?

A. This question, any more than many others I have already answered, can have no reference to the pretended plot.

Mr. Pitt. That does not signify; you are bound by the oath you have taken to answer it. To Mr. Fawkener. Read the oath. (The oath read.)

Mr. Atty. Gen. You perceive, Sir, you have sworn to true answer make to such questions as shall be put to you respecting certain matters before this board.

A. But it was surely agreed that I was to object to certain questions.

Mr. Atty. Gen. Yes, to such as might criminate yourself, and to those only.

Mr. Pitt (with great petulancy). Repeat the question and take down his answer.

Mr. Atty. Gen. Choose whether you will answer the question, or take the consequences of a refusal.

Mr. Pitt. Aye! Aye!

Mr. Atty. Gen. Now, Sir, where did you see Hodgson?

A. I wish not to behave with incivility towards your Lordships. But I must say, and that not without considering my answer, that I am used exceedingly ill.

Mr. Pitt. What can you mean, Sir; by whom?

A. By this Board. My Lords, I understood I was to be interrogated respecting one particular matter, and the question now put can have no reference to it.

Mr. Pitt. Sir, you cannot object to this question?

A. I conceive that I *can*, and *do* on this ground also—that you ought not to put such questions, the refusing to answer which will imply crimination.

Mr. Atty. Gen. Sir, you must answer the question.

One of their Lordships. Unless it will criminate yourself.

A. My Lords, my legal knowledge is but very trifling; it chiefly consists in knowing what was crime a few years ago; but from the extraordinary circumstances I have lately observed, I know not what may be now deemed crime or not. On that ground also I object to answering this question.

Mr. Atty. Gen. Then, Sir, you know that a bill was found yesterday, for High Treason against Hodgson, by a Grand Jury of his countrymen?

A. I learned so from the public papers, and indeed, from himself.

Mr. Atty. Gen. Now, Sir, if after that you conceal him, you are guilty of Misprision of Treason.

A. That, Sir, I am aware of.

Mr. Atty. Gen. Now, Sir, answer the question; but you are not wished to criminate yourself.

A. Then, I saw him *in my own house.*

Mr. Atty. Gen. At what time?

A. About eleven in the evening.

Q. What did he come about?

A. Nothing particular; he laughingly told me of the bill found against him.

Q. At that time of night—you think that was late, don't you?

A. No.

Q. Why, he did not come to you in the way of your profession, did he?

A. No.

Q. Why, do you have visitors even at that late hour?

A. Yes, often my Lords, I sit up late.

Q. How long did he stay?

A. About ten minutes.

Q. What place had he been at last before you saw him?

A. Must I answer that question?

Mr. Atty. Gen. Yes, certainly.

A. At a public house.

Q. Where, there are many public houses?

A. In Shoreditch.

Q. Whereabouts, Shoreditch is a large place, is it not?

A. Near the church.

Q. Near the church, Sir; but what sign was it?

A. Am not quite sure; it was a public-house facing the church.

Q. Why, is there more than one?

A. Yes.

Mr. Pitt. What sign do you suppose it was, Mr. Parkinson?

A. I think it must have been either the King's Arms, or the Star and Garter. (Here Mr. Pitt wrote down a few words on a slip of paper, and carried them out of the room.)

Q. Do you know where he is now?

A. No.

Q. Do you know where we can find him?

A. No.

* * * * * * * *

Q. Pray, Sir, did you ever see one of these pamphlets? (*The Vindication of the London Corresponding Society.*)

A. Yes, my Lords.

Q. Do you know the author?

A. Exceedingly well.

Q. Who is the author?

A. I object to the question.

Q. You cannot object to it unless it will criminate yourself. —Who is the author?

A. I object to the question.

(One of their Lordships to Mr. Fawkener.—Put down—Refuses to answer, *because* it will criminate himself.)

Irritated by this attempt to foist the words of another into my examination, I struck my hand on the table and said,—My Lords, I claim that no words be inserted in my examination as my answers but what proceeds from my own lips—I gave no such reason.

(Another of their Lordships. Only put down refuses to answer this question.)

A. The question, my Lords, is not in itself worth contention. If put again I will answer it.

Q. Who is the author?

A. I am the author.

Q. You are the author?

A. I am the author.

Q. And pray, was this intended to be published before the trials?

A. It was.—But on its being suggested, I believed by myself, that it might be not proper, it was resolved it should not, the press was therefore stopped.

Q. How many were printed then?

A. Only two hundred and fifty.

Q. How many had been intended?

A. I think two thousand.

This letter also shows that Parkinson wrote to the Privy Council in behalf of one of the accused, John Smith, who had been thrown into Newgate prison on the treason side, and who though ill at the time was left exposed to wet and cold in a most atrocious manner and consequently became seriously ill. As a result of Parkinson's intervention, Smith was moved into more tolerable apartments and was given medical attendance.

Though an agitator and reformer, Parkinson found great fascination in geology and even more particularly in the study of paleontology and oryctology. Little was known of these sciences in England at that time, but he entered this field with keen interest and enthusiasm. He became one of the original

members of the London Geological Society, his attention being chiefly centered in the study of the organic remains of former ages as they existed in the various strata in and around London. He was an enthusiastic student and collector. His collection grew and became famous, and he contributed numerous articles to the leading scientific journals. His knowledge of and interest in these subjects is shown in his important work entitled "Organic Remains of a Former World." This consists of three large volumes, which it took him several years to prepare, the first volume appearing in 1804, the second in 1808, and the third in 1811.

In 1822 he published "Outlines of Oryctology," or an introduction to the study of fossil organic remains. This is a book of 340 pages which served for some time as a text book. It passed through three editions. From a study of the title page we see that Parkinson was a member not only of national but of foreign geological societies.

The importance of his contributions to geology, paleontology and oryctology is proven by citations from the writings of one of England's greatest paleontologists who wrote half a century later. In 1850 Mantell published "A Pictorial Atlas of Fossil Remains," which consisted of illustrations selected chiefly, he tells us, from Parkinson's "Organic Remains of a Former World." In the introduction Mantell says:

> The publication of Mr. Parkinson's 'Organic Remains of a Former World' at the commencement of the present century must be regarded as a memorable event in the history of British paleontology. It was the first attempt to give a familiar and scientific account of fossil relics of animals and plants accompanied by the figures of the specimens described.
>
> The three volumes of which the work consisted appeared at considerable intervals; the last was published in 1811, although nearly forty years have since elapsed and hundreds of geological works of all kinds and degrees of merit have subsequently been issued, Mr. Parkinson's plates, owing to their fidelity and beauty, are still in such request as to induce the proprietor, Mr. Bohn, now that the work is out of print, to publish them, with the descriptions and modern names of the fossils represented.

Chemistry also proved an attraction to him and he seems to have foreseen its wonderful possibilities in relation to scientific medicine. He studied chemistry for its own sake as well as for its application to medicine. The results of his study took tangible form and appeared in a little book entitled "The Chemical Pocket-book"[2] which represented the inorganic and physiological chemistry of that day.

His remarks on caloric are of interest, as showing how intelligent and well informed he was for his time. He says:

> Heat, with the various changes produced by it in bodies, is considered by some, as merely the consequence of certain mechanical changes in bodies, but it is most generally supposed that these effects depend on a certain matter called caloric or the matter of heat.
>
> Caloric appears to be an highly elastic imponderable fluid, and is so very subtle, that neither has its gravity been yet ascertained, nor its existence, in a simple and uncombined state been shown. It combines chemically with all bodies, in a quantity proportioned to their affinity with it. By its elastic power it constantly tends to separate the particles of matter in which it is opposed by the attraction of cohesion, hence attraction of cohesion predominating the body exists in a solid form, caloric existing in such a proportion as to weaken the attraction of cohesion to a certain degree, the body assumes a liquid form, and when the quantity of caloric is increased still further, the body takes a gaseous form.
>
> It constantly tends to form an equilibrium, by passing from bodies of an higher, and diffusing itself through bodies of a lower temperature.
>
> * * * * * * * *
>
> Count Rumford, from the great quantity of heat produced by friction, is induced to ask, What is heat? Is there any such thing as the aqueous fluid? Is there anything that can with propriety be called caloric? He observes the source of heat generated by friction appears evidently to be inexhaustible, and adds, that anything which any insolated body, or system of bodies can continue to furnish without limitation, cannot possibly be a material substance.
>
> Heat, Mr. Davy says, or that power which prevents the actual contact of the corpuscles of bodies, and which is the cause of our peculiar sensations of heat and cold, may be defined as a peculiar motion, probably a vibration of the corpuscles, tending to separate them. It may with propriety be called the Repulsive Motion. The non-existence of caloric or fluid of heat, he thinks his experiments have proved.
>
> Dr. Beddoes is also of the opinion that most of the phenomena relative to heat, are more readily reconcilable to the mechanical rather than to the chemical doctrine of heat.

In this chemistry he describes the character of the elements, their compounds, etc., in the ordinary text-book style; and the last thirty pages are devoted to the physiological chemistry of "Animal Substances," such as the blood, gastric and other internal juices, and secretions of the body, bones, teeth, shells, eggs and feathers of birds, etc., etc.

The small volume was apparently very popular, for it ran through several English and American editions.

An entirely different side of his life is revealed in a book entitled "*Dangerous Sports*[3]—a tale addressed to children warning them against wanton, careless or mischievous exposure to situations from which alarming injuries so often proceed." This to the writer appears as the most peculiar of

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[2] *The Chemical Pocket-book; or Memoranda Chemica;* arranged in a Compendium of Chemistry, with tables of attractions, etc. Calculated as well for the occasional reference of the professional student as to supply others with a general knowledge of chemistry, by James Parkinson, with the latest discoveries, from the London second edition of 1801, to which is now added An Appendix containing the principal objections to the antiphlogistic system of chemistry, by James Woodhouse, M. D., professor of chemistry in the University of Pennsylvania, etc. Philadelphia. Printed and sold by James Humphreys, at the N. W. corner of Walnut and Dock St., 1802. First American edition, 1799. On its last page is the following announcement:

Dr. Woodhouse's Lectures on Chemistry commence on the first Tuesday in November of every year, in the city of Philadelphia, and end on the last day of February.

He possesses a complete chemical apparatus, and during the course, several thousand brilliant experiments are exhibited.

Specimens of the various earths, salts, ores of metals, etc., are shown to the class.

[3] The first edition was published in 1800, the second in 1808.

all his writings. The title might better have been "Don'ts for Children." The advice consists of a succession of "don'ts," frequently repeated, with examples appended of disastrous results accruing from a failure in the past to observe the cautions and precautions laid down by the story-teller.

The reader is introduced to an old cripple called Millson who finds a child terribly hurt from an accident which occurred as a result of boys throwing stones at the horse upon which the child had been riding. Millson looks after the child and returns him to his home, for which he enjoys the gratitude of both the child and parents. The writer then warns boys never to scare a horse or to throw stones at one, particularly when anyone is riding it. He also warns children not to strike strange dogs and tells them how best to meet an attack of a ferocious dog.

The next part in which he represents a house-party for children to which old Millson is invited is still more peculiar. Old Millson appoints himself professor of sport and undertakes to teach the children how to play without exposing themselves to danger and how they ought to enjoy themselves by learning something of electricity or by magic lantern pictures, etc.

The plan of teaching is as follows: One of the party does something which exposes someone to danger, whereupon old Millson calls them all together and then relates the incident, drawing morals for them. Next he tells them a story of a similar action with a very disastrous ending and then tells them not to do it again.

The subjects with which old Millson deals include all the things which add spice to the life of a child. He advises the boys never to stand too close to the batter in a cricket game, never to climb trees or rob birds' nests, never to risk life or limb in playing stump or follow the leader, never to throw stones or go swimming in deep water, never to go out on thin ice, or to play with pistols or even with bow and arrows, never to close a penknife against the thigh, to taste unknown substances or to cut the end off of a cripple's crutch, etc. Intended to entertain children, one can imagine how they must have enjoyed it! The book doubtlessly found more favor among parents. Certainly the advice contained in it would never develop the best part of a boy's nature, and if accepted would certainly rob the world of all its Tom Sawyers.

The son of a doctor, reared in the home of a practicing physician, Parkinson entered the profession with a full knowledge of what the practice of medicine meant and of the nature of the life of a general practitioner. In his early life he studied shorthand, which proved later of great service to him in the course of his studies. After graduation he still continued to be a student, taking courses in those branches which particularly appealed to him, for he was ambitious. A careful student of the philosophy and progress of his age, a trained thinker, he did not accept as truth anything lacking in scientific proof, entering into many arguments and controversies with his contemporaries.

The fact that he was a fellow of the Royal College of Surgeons stamps him as a man of learning and of standing in the profession; while the large number of his publications bears witness to his industry.

A most peculiar side of his nature is revealed in the publication of medical books for the laity which somewhat resemble the household medical books or home practitioners of today. It is difficult to understand why he wrote them. The prefaces and introductory remarks pretend to convey his reasons to the reader but these impress one as being exceedingly apologetic in nature, as though the author felt some compunction concerning the publication of these works and found it difficult to convince himself by arguments that it was absolutely proper and advisable that he should publish them. Whatever his feelings were, the books did appear.

Hints for the Improvement of Trusses[4] is a pamphlet of twenty-two pages. The author offers some original ideas as to home methods that may be used to keep a hernia in place. He gives as his reason for writing this book that he does not believe in exclusive patents and wants to make the idea widespread for general use by the poor.

> Possessing these sentiments respecting the reservation of exclusive property, in those discoveries which conduce to the preservation of life, and the diminution of disease, it was sufficient to believe it possible, that the present little improvement might, eventually, prove beneficial, to produce such a publication of its description, as might prevent anyone assuming the principle as their discovery, for the purpose of obtaining an exclusive patent. By stating this, however, it is not meant to arrogate the merit of a very important discovery, it is merely offered as a hint, which may probably suggest means of relief, easy of acquisition, in a disease in which, if these or similar means be omitted, a fatal termination may be expected to occur. A hope is also entertained that the principle, capable of being further extended, may, under the attention of the ingenious mechanic, or even of the patient himself, be so modified, as to be applied to the construction of an instrument, still more simple and more efficacious than any which have been, as yet, adopted.

The occasion for the appearance of a book entitled "Mad Houses"[5] was a series of attacks by newspapers and by one "short-lived medical newspaper" against him for his seeming neglect before signing the papers which committed Mary Daintree to confinement for insanity. In this pamphlet of thirty-eight pages he discusses first, the laws for confinement, then shows their weak points and suggests ways of remedying their shortcomings.

> The miseries of any one unnecessarily consigned to the horrors of a mad-house, and the state of the unhappy lunatic, whose

[4] Hints for the Improvement of Trusses intended to Render their Use less inconvenient and to Prevent the Necessity of an understrap, with the Description of a Truss of Easy Construction and Slight Expense for the Use of the Labouring Poor, to whom this little tract is chiefly addressed. By James Parkinson. Hoxton. Price nine pence. 1802.

[5] Mad Houses. Observations on the act regulating mad-houses and a correction of the statements of the case of Benjamin Elliott, convicted of illegally confining Mary Daintree, with remarks addressed to the friends of insane persons. By Jas. Parkinson. 1811.

privation of reason leaves him without the power of complaint against those, who, false to their trust, may augment instead of diminish his sufferings, alike excite our commiseration. We cannot, therefore, but look with gratitude to the labours of those who brought forward that act, the objects of which are, the regulation of mad-houses, the admission of patients, and the visitation of these houses and patients by proper persons.

But here, as in many other instances, the first endeavors of benevolence have not been fully successful. Although the grand points, which the authors of the bill had in view, are in a great measure obtained, other less evils remain unabated, and some exist which are the consequence of imperfections in the bill itself. To point out these evils, and to endeavor to trace them to their true source, and to suggest means by which they may be removed or lessened, are the objects of the present attempt.

In the last ten pages he goes over his evidence given at the trial of relations who were instrumental in the commitment of Mary Daintree, confined for three months in a madhouse, from which it would appear that he had fully done his duty and that he was justified in signing the bill of commitment. It appears that his evidence was wrongly quoted in the newspaper and as he did not take the trouble to correct this paper it was quoted by other papers and severe criticism had been passed on his conduct in the affair.

Parkinson states in the trial that he is visiting surgeon of the madhouse. This publication appeared two months after the trial and was sold to the public for two shillings.

Probably the most interesting part of his book entitled "Medical Admonitions"[6] is the introduction to the table of symptoms, in which the author outlines his position and offers a reason for undertaking the publication of a book on medicine intended for circulation and use among the laity. He says:

Should any one obstinately put to sea without a compass to steer by and without any knowledge respecting the navigation of a ship, but what he picks up during his voyage, by reference to some treatise on navigation, it would not be sufficient, merely to endeavor to dissuade him from making the rash attempt. But if he persist, every profitable assistance should be yielded him, the perils he has to shun should be clearly pointed out, the different rocks and quicksands he is to avoid should be marked, and the different circumstances should be described which may show his near approach to danger. With a similar intention is the following table given.

Then follows a list which includes every conceivable symptom, what the purport of these symptoms may be and suggestions as to the seriousness of the case. This occupies some forty-three pages.

This book like so many of the Home Practitioners is a brief, concise picture of different diseases, with an outline of treatment, and a statement as to the gravity, etc. It comprises about 500 pages and deals with nearly all the recognized medical diseases.

In "The Villagers' Friend"[7] he represents himself as an old practitioner who has been the village apothecary for thirty years, during which time he has labored long and hard and has received little in return, and now in his old age he is poored than when he started practice. He is leaving practice to devote the remainder of his days to some rustic employment. In parting he advises his old friends and patients. The reader is reminded of how little the public has considered the comfort or pleasure of its physician, of the nights spent in buffeting stormy elements in response to urgent calls for which no necessity existed, and he tries to inculcate some consideration on the part of the reader for the comfort and well being of the physician of the future. He deals with the value of exercise as a therapeutic measure, warns against the dangers of drink, advises thrift but not overwork. Bathing is advocated as a prophylactic measure, but not a cure for disease, for he is afraid of its employment during the course of disease.

Throughout this volume the Friend delights to use proverbs and Parkinson here really appears as a medical Sancho Panza. The book was very highly recommended by the press in general and by several medical journals, for example, the Medical and Physical Journal, The London Medical Review and Magazine, and Medical and Chirurgical Review.

Our greatest interest, however, is centered in his contributions to medicine itself. What did he do that appealed to the profession? What did he contribute to medical science?

Gout in his day was the same difficult but attractive problem that it is today. It was known to be in some way associated with uric acid. It appealed from the chemical side to him and also from the side of treatment probably, as he himself was a sufferer from this disease.

Parkinson had some ideas concerning gout, its cause and treatment, and he was very definite about them. Another gentleman, Dr. Kinglake, equally confident also had ideas on this subject and had written a large book on the subject. Parkinson's ideas, however, did not exactly coincide with those of Kinglake, so that gout furnished then, as it can now, an excellent subject for a controversy.

In 1805 his book entitled "Observations on the Nature and Cure of Gout"[8] appeared. Parkinson states in the preface that he had frequently felt urged to write on this disease, from which he himself had suffered so greatly, but for various reasons he had not done so. "But the perusal of Dr. King-

[6] Medical admonitions to families respecting the preservation of health and the treatment of the sick. Also a Table of Symptoms serving to point out the degree of danger and to distinguish one disease from another, with observations respecting the improper indulgence of children. By James Parkinson, M. D. Hoxton. First American from the fourth English edition. 1803.

There were five editions of this work published between 1799 and 1809.

The volume that I was privileged to see was from the library of Dr. Pierre Chatard and was the gift of Dr. Ferdinand E. Chatard to the library of the Johns Hopkins Hospital.

[7] The Villager's Friend and Physician, or a familiar address on the preservation of health, and the removal of disease, on its first appearance; supposed to be delivered by a village apothecary; with cursory observations on the treatment of children, on sobriety, industry, etc., intended for the promotion of domestic happiness. By James Parkinson. 1800. Small volume of 85 pages. Cost 1 shilling.

[8] Observations on the nature and cure of gout, etc. 8°. London. N. D. Symonds, 1805.

lake's 'Dissertation on Gout'[9] determined my intentions. Strongly suspecting that the advice delivered in that work, with so much benevolence and zeal, must in many instances prove highly injurious, and believing that the observations which I had made might serve to prevent too general an adoption of that advice, I resolved on their publication."

It is interesting to note that he advises against the use of the Duke of Portland powder and quotes Cadagon who says, "I myself observed between fifty and sixty of its advocates, some my patients, some my acquaintances or neighbors, who were apparently cured by it, but in less than six years' time *'omnes ad internecionem cæsi,'* they all died to a man." He also quotes Cullen who said that in every instance which he had known of the exhibition of this medicine for the length of time prescribed, the persons who had taken it were indeed afterwards free from any inflammatory affection of the joints, but they were affected with many symptoms of the atonic gout, and all, soon after finishing their course of the medicine, have been attacked with apoplexy, asthma or dropsy, which proved fatal. He strongly criticises Dr. Kinglake's writings and states that application of cold produces irregular or retrocedent gout (in the viscera), which is more to be dreaded than joint gout. Indeed in the irregular form of gout fermented liquors were administered in order to increase it to such an extent that the joints would become affected and the disease become localized and leave the internal viscera free.

In one part he refers to the observation of Heberden,[10] "The doctor speaks of these tumors, as existing only on the third joints of the fingers which may be accounted from the circumstance of their almost always making their first appearance on these joints, some months and even sometimes years elapsing before they appear on the second series of joints. Although it is undoubtedly a fact, that they are often to be found on those persons to whom gout is unknown, yet they often exist where gout has manifested itself, in some slight attack, at some former period." Parkinson also says they may be painful. He evidently does not distinguish between gout and arthritis deformans or hypertrophic arthritis, for he says that "the disease noticed by Dr. Heberden is the same to which this chapter is devoted."

Two years following the appearance of Parkinson's book on gout, Kinglake retaliates with another pamphlet.[11]

In the preface Kinglake states that the contents of this work were originally intended for another volume which was a reply to the hosts of criticisms mostly anonymous, but "Mr. Parkinson's manly and open criticism was worthy of separate reply."

[9] A dissertation on gout, etc. 8°. London. J. Murray. 1804.

[10] Commentarii de morborum historia et curatione. 8°. London. T. Payne. 1804.

[11] Strictures on Mr. Parkinson's observations on the nature and cure of gout, recently published in opposition to the theory, that proposes the cooling treatment of that disease: to which are added in an appendix two letters addressed to Dr. Haggarth, containing remarks on the opinions he has lately published, on acute rheumatism, the use of cinchona or Peruvian bark in that disease, and on what he terms "nodosity of the joints." 8°. Taunton. J. Poole. 1807.

Each part of Mr. Parkinson's book which deals with fundamental principles, of the cause and treatment of gout, is taken up and discussed.

Mr. Kinglake does not agree with the chemical theory but he speaks of "its practical importance, were it capable of being established." He becomes sarcastic, "but it would seem that the respective discoveries of Scheele, Forbes, Pearson, Fourcroy and Wollaston attracted the admiration of Mr. Parkinson, and induced him to meditate the fabrication of a theory of gout, more chemical, more scientific, more worthy the suffrages of the learned world, and perhaps more politic, too, than any view of the disease possibly could be, that would authorize the topical use of cold water." He scores heavily on Parkinson who thinks that wine and punch, not beer and malt, are the greatest exciting etiological factors, when he observes that he has found gout more prevalent in those who from habit or preference use malt liquor for common beverage.[12]

Kinglake criticises very strongly the interpretation placed on observations made by Parkinson, ridicules his array of cases in which the harmful effect of the application of cold are detailed (only one of which was treated with cold and here the result was good and the symptoms appearing a year later cannot possibly be the result of the treatment given). "Less integrity and more art might have given them a more imposing appearance, but Mr. Parkinson's regard for truth has conferred on them no more than their real value."

He ends by complimenting Parkinson on his book. "It would be tacit detraction in me to terminate my strictures on Mr. Parkinson's work, without acknowledging it to be on the whole a medical performance of the first class of respectability. Although indeed, it is not in my power to assent to the hypothesis it contains, it is but just to say, that like the author's other publications, it at once abounds with proof of reputable talent and of an amiable disposition to benefit mankind."

The library of the British Museum contains a small work entitled "Observations on Dr. Hugh Smith's Philosophy of Physic." This was published in 1780, and has always been ascribed to Parkinson. On the fly leaf is written "From the author with his most respectful compliments." The "Observations" are addressed to Hugh Smith, M. D. of Hutton Street. "These observations, Sir, are dedicated to you, with that earnestness, which the subject demands, that deference, which is due you, and that diffidence, which ought to accompany an opposition to opinions, which are said to be founded on experiments and confirmed by physiological researching and the closest method of reasoning."

"By their fruits ye shall know them." Although written anonymously, this is almost certainly Parkinson's work. The method of presenting the subject matter, the arguments themselves, and the style of speech are strikingly suggestive. The preface and introduction, full of compliments and praise for Dr. Smith and the unsparing attacks on Smith's work itself,

[12] In treatment Parkinson advises the total avoidance of fermented liquors except in atonic gout.

have their analogue in Mr. Parkinson's attitude toward Kinglake in "Observations on the Nature and Cure of Gout."

The first chapter is devoted to refuting Smith's definition of a gland and to a discussion of so-called "Vital Air," which according to him is responsible for the circulation of the blood. Parkinson can see no difference between ordinary air and vital air and denies that it has anything to do with circulating the blood.

He shows that Dr. Smith has gone at great length into a contraversion of Boerhaave's theory of circulation which, Parkinson says, for thirty years has not been accepted by leaders in medicine. Smith had attacked it as though it still was standing and gave no credit to Cullen and others who had refuted it in part. Parkinson recalls all this and then discusses some of Smith's criticisms which he says have not attacked the theory in its assailable parts but in the parts where it stands firm and is still accepted. He says also that Smith has not interpreted Boerhaave properly. Smith claimed that he had experimental proof that heating of air in fluid in close confinement in tubes caused circulation. Parkinson asks him for demonstrations or for records of such experimental proof.

In observations of the second chapter of "Philosophical Inquiries" it is shown that Boerhaave claimed that "the air by distending the vesicles of the bronchi compresses the veins in inspiration and hence the air cannot, at this time, gain entrance into the pulmonary veins."

Smith claimed that "the power of any given quantity of air is abated in proportion as it is divided and subdivided into parts that are asunder from each other," and that "the innumerable cells of the bronchi seem admirably contrived by the author of nature to prevent this compression."

Parkinson says that this idea is false, as air in subdivision is exposed to a much greater heating surface and consequently expands more rapidly and exerts more compression than if it were not distributed to the various vesicles and alveoli.

He also rejects on physical grounds Smith's idea that a cutaneous respiration exists—Smith claiming that the vital air is increased by heavier air entering through the skin and lighter air and excrementous fluids passing out through it at one and the same time.

The "Hunterian Reminiscences"[13] are doubly interesting because they reveal the opinion of Parkinson concerning Hunter and furnish us with a full set of Hunter's lecture notes.

Preface.—To those gentlemen who have been instrumental, by their solicitations, to the production of this work, and who are aware of the motives which induced the editor to present it to his medical brethren, any preface or introduction may appear uncalled for, if not superfluous. But by those who have the good fortune to be now commencing the study of their profession under the direction of the enlightened professors of the present day, not only in every branch of medicine, but in every science associated with it, a few prefatory observations may be deemed requisite; for to them the necessity or utility of publishing the substance of lectures delivered half a century ago may not be apparent.

Nor is the absolute necessity or utility contended for: no more would it be necessary to examine the foundation of a building, every part of whose superstructure bespeaks its stability; yet it is pleasing, nay, highly interesting, occasionally to descend from the height to which modern surgery has attained, and carefully retrace each step, until we arrive at the very base on which it rests, every stone of which may be said to be inscribed with the name of John Hunter, for not only did he supply the materials, and work them with his own hands; but, if proof were wanting of how much he left wherewith to adorn the superstructure, let us visit the far-famed Hunterian Museum, where we may take our stand, and exaltingly exclaim 'Si monumentum quaeras, circumspice.

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With all its faults, for many of which the Editor holds himself personally accountable, he trusts the work will, in some measure, supply the loss which surgical science has sustained by the destruction (by accident it is to be hoped) of the original notes from which Mr. Hunter lectured. With this view alone does he deliver it into the hands of a learned and liberal profession, to be dealt with according to its merits.

In 1817 he wrote his "Essay on Shaking Palsy."[14] This constitutes his greatest and most important contribution to medicine. It alone is responsible for the handing down of his name to posterity and without it, his name would have died with him.

In the preface he states:

The disease, respecting which the present inquiry is made, is of a nature highly afflictive. Notwithstanding which, it has not yet obtained a place among nosologists; some have regarded its characteristic symptoms as distinct and different diseases, and others have given its name to diseases differing essentially from it; whilst the unhappy sufferer has considered it an evil, from the domination of which he had no prospect of escape.

The disease is of long duration: to connect, therefore, the symptoms which occur in its later stages with those which mark its commencement, requires a continuance of observation of the same case, or at least a correct history of its symptoms, even for several years. Of both of these advantages the writer has had the opportunity of availing himself; and has hence been led particularly to observe several other cases in which the disease existed in different stages of its progress.

His definition of the disease is as follows:

Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellects being uninjured.

He credits Galen with having distinguished two forms of tremor, one which occurs during attempts at movement, and the other while the parts are at rest, to the latter of which the term palpitation was applied. Sylvius de la Boë, Juncker, Cullen and Sauvages are also credited with distinguishing

[13] Hunterian Reminiscences being the Substance of a Course of Lectures on the Principles and Practice of Surgery delivered by the late Mr. John Hunter in the year 1785. Taken in shorthand and afterwards fairly transcribed by the late Mr. James Parkinson. Edited by his son, J. W. K. Parkinson, F. R. C. S., Lond.

[14] An essay on shaking palsy. 8°. London. Sherwood, Neely & Jones. 1817.

various forms of tremor. "Tremor has been adopted, as a genus, by almost every nosologist; but always unmarked in their several definitions, by such characters as would embrace this disease."

The following quotation is somewhat long but the description of the disease is so good that it should be better known by physicians, and we therefore venture to reprint it:

So slight and nearly imperceptible are the first inroads of this malady, and so extremely slow is its progress, that it rarely happens, that the patient can form any recollection of the precise period of its commencement. The first symptoms perceived are a slight sense of weakness, with a proneness to trembling in some particular part; sometimes in the head, but most commonly in one of the hands and arms. These symptoms gradually increase in the part first affected; and at an uncertain period, but seldom in less than twelve months or more, the morbid influence is felt in some other part. Thus assuming one of the hands and arms to be first attacked, the other, at this period becomes similarly affected. After a few months the patient is found to be less strict than usual in preserving an upright posture: this being most observable whilst walking, but sometimes whilst sitting or standing. Sometime after the appearance of this symptom, and during its slow increase, one of the legs is discovered slightly to tremble, and is also found to suffer fatigue sooner than the leg of the other side: and in a few months this limb becomes agitated by similar tremblings, and suffers a similar loss of power.

Hitherto the patient will have experienced but little inconvenience; and befriended by the strong influence of habitual endurance, would perhaps seldom think of his being the subject of disease, except when reminded of it by the unsteadiness of his hand, whilst writing or employing himself in any nicer kind of manipulation. But as the disease proceeds, similar employments are accomplished with considerable difficulty, the hand failing to answer with exactness to the dictates of the will. Walking becomes a task which canot be performed without considerable attention. The legs are not raised to that height, or with that promptitude which the will directs, so that the utmost care is necessary to prevent frequent falls.

At this period the patient experiences much inconvenience, which unhappily is found daily to increase. The submission of the limbs to the directions of the will can hardly ever be obtained in the performance of the most ordinary offices of life. The fingers cannot be disposed of in the proposed directions, and applied with certainty to any proposed point. As time and the disease proceed, difficulties increase: writing can now be hardly at all accomplished; and reading, from the tremulous motion, is accomplished with some difficulty. Whilst at meals the fork not being duly directed frequently fails to raise the morsel from the plate, which, when seized, is with much difficulty conveyed to the mouth. At this period the patient seldom experiences a suspension of the agitation of his limbs. Commencing, for instance in one arm, the wearisome agitation is borne until beyond sufferance, when by suddenly changing the posture it is for a time stopped in that limb, to commence, generally, in less than a minute in one of the legs, or in the arm of the other side. Harassed by this tormenting round, the patient has recourse to walking, a mode of exercise to which the sufferers from this malady are in general partial; owing to their attention being thereby somewhat diverted from their unpleasant feelings, by the care and exertion required to ensure its safe performance.

But as the malady proceeds, even this temporary mitigation of suffering from the agitation of the limbs is denied. The propensity to lean forward becomes invincible, and the patient is thereby forced to step on the toes and forepart of the feet, whilst the upper part of the body is thrown so far forward as to render it difficult to avoid falling on the face. In some cases, when this state of the malady is attained, the patient can no longer exercise himself by walking in his usual manner, but is thrown on the toes and forepart of the feet; being at the same time, irresistibly impelled to take much quicker and shorter steps, and thereby to adopt unwillingly a running pace. In some cases it is found necessary entirely to substitute running for walking; since otherwise the patient, on proceeding only a very few paces, would inevitably fall.

In this stage, the sleep becomes much disturbed. The tremulous motion of the limbs occur during sleep, and augment until they awaken the patient, and frequently with much agitation and alarm. The power of conveying the food to the mouth is at length so much impeded that he is obliged to consent to be fed by others. The bowels, which had been all along torpid, now, in most cases, demand stimulating medicines of very considerable power: the expulsion of the fæces from the rectum sometimes requiring mechanical aid. As the disease proceeds towards its last stage, the trunk is almost permanently bowed, the muscular power is more decidedly diminished, and the tremulous agitation becomes violent. The patient walks now with great difficulty, and unable any longer to support himself with his stick, he dares not venture on this exercise, unless assisted by an attendant, who walking backwards before him prevents his falling forwards, by the pressure of his hands against the forepart of his shoulders. His words are now scarcely intelligible; and he is not only no longer able to feed himself, but when the food is conveyed to the mouth, so much are the actions of the muscles of the tongue, pharynx, etc. impeded by the impaired action and perpetual agitation, that the food is with difficulty retained in the mouth until masticated; and then as difficultly swallowed. Now also, from the same cause, another very unpleasant circumstance occurs: the saliva fails of being directed to the back part of the fauces, and hence is continually draining from the mouth, mixed with the particles of food, which he is no longer able to clear from the inside of the mouth.

As the debility increases and the influence of the will over the muscles fades away, the tremulous agitation becomes more vehement. It now seldom leaves him for a moment; but even when exhausted nature seizes a small portion of sleep, the motion becomes so violent as not only to shake the bed-hangings, but even the floor and sashes of the room. The chin is now almost immovably bent down upon the sternum. The slops with which he is attempted to be fed, with the saliva, are continually trickling from the mouth. The power of articulation is lost. The urine and fæces are passed involuntarily; and at the last, constant sleepiness, with slight delirium, and other marks of extreme exhaustion announce the wished-for release.

Histories of six cases are given; the subject in each instance being a man of advanced age—in the five cases in which the age is mentioned the patient being above fifty years. Only two of the cases are absolutely typical, three others were only met with casually in the street, the opportunity of studying the objective features of the disease having been eagerly seized.

The attitude, the weakness, the tremor and the gait are accurately described, the rigidity is strongly suggested, particularly by one line, "the chin is now almost immovably bent down upon the sternum," while elsewhere the clumsiness and incoordination are more emphasized than is rigidity.

Nowhere in this essay is a description of the "mask" face—the so-called Parkinson face—encountered. It is possible that later he drew attention to the "mask" face but cer-

tainly no justification for the term "Parkinson's mask" can be found in his original essay.

Attention is called to the fact that the festinant gait (*scelotyrbe festinans*) had been previously noted and described by Carguet, by Gaubius and by Sauvages, although its association with the other symptoms in the symptom complex had not been recorded.

The question of differential diagnosis from other palsies, from anomalous forms of Jacksonian epilepsy, from hysteria, delirium tremens and tremors incident upon excessive use of tea, coffee and alcohol, is also considered.

In discussing the etiology he offers only apologies, as no autopsy had been made on any of the cases. He hesitatingly advances some conjectures and opinions which he admits are but sorry substitutes for facts, and points out that none of the symptoms of the disease are encountered in patients suffering from compression, laceration or complete division of the spinal cord. He thinks, however, that the seat of the disease is probably in the upper cord and extending as the disease progresses up into the medulla.

It is suggested that early treatment may be able to check the progress of the disease—bleeding, vesicatories and linaments and an issue (he is specific) one and one-quarter inches, at least, in length being advised. He assumes a hopeful attitude for such measures but thinks that internal remedies will be without avail.

The numerous citations from his writings disclose his style more adequately and much better than any description possibly could. One is often tempted to read on not so much because of the matter as because of the somewhat unusual and interesting method in which he reveals his ideas. He is verbacious and his sentences are complicated but readily understood. This peculiarity is common to all his writings.

Much can be surmised as to his personal character from a study of his varied writings. Certain characteristics stand out strongly, his love of controversy, his love of admonishing those about him, his love of freedom of speech and writing, and his deep interest in the various branches of science, as chemistry, geology and medicine. Fortunately all is not left to surmise. Mantell furnishes us with a description of his physical and social nature.

> I gladly avail myself of this opportunity to make a passing allusion to the excellent and accomplished author, Mr. Parkinson. I had the pleasure and the privilege of his acquaintance in my youth, immediately after the publication of the third volume of his valuable work. Mr. Parkinson was rather below the middle stature, with an energetic, intelligent and pleasing expression of countenance and of mild and courteous manners; readily imparting information either on his favorite science or on professional subjects; for he was at that time actively engaged in medical practice in Hoxton Square and was the author of several valuable medical treatises. . . . "
>
> . . . In after years Mr. Parkinson warmly encouraged my attempts to elucidate the nature of the strata and organic remains in my native county, Sussex, a district which was then supposed to be destitute of geological interest and he revised my drawings and favored me with his remarks on many subjects treated of in my first work.

He also speaks of the attractive style of Parkinson, in proof of which he quotes a whole chapter from one of Parkinson's books on geological subjects.

Parkinson died during his sixty-ninth year on December 21, 1824, in Kingsland Road and was buried on December 29, 1824. Until death he remained a parishioner of Hoxton and was buried in the parish burying grounds, the churchyard of St. Leonard's Shoreditch Church, the entry appearing in the parish register. In later years many of these graves were disturbed, the stones being lost. No stone bearing his name can be found in the old churchyard.

What then did Parkinson accomplish during his life? He cannot be considered a brilliant investigator and certainly he made no startling contributions to science. He was a man of the Old Master type described by Holmes rather than the highly specialized scarabaeist. Master of medicine, chemistry, geology, paleontology and oryctology, he was a writer of many textbooks, great as a compilator, keen in observation and desirous of seeing everything named and placed in its proper class. His most important contribution to medicine was the offspring of the last two qualities.

He was a member of the Geological Society of London, the Wernerine Society of Edinburgh, and of the Caesarean Society of Moscow, a Fellow of the Royal College of Surgeons.

'Tis true his chief contribution to medicine consisted simply in describing a disease and giving it a name, thereby establishing it as a clinical entity. It may be argued that he neither discovered its etiology nor found a cure; but the disease has stood an open challenge to investigators for a full century. "Let him that is without sin cast the first stone."

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IS THE ANASTOMOSIS BETWEEN THE PORTAL VEIN AND THE VENA CAVA COMPATIBLE WITH LIFE?

By B. M. Bernheim, M. D.,
Assistant in Surgery
and
Carl Voegtlin, Ph. D.,
Associate Professor of Pharmacology.

(From the Hunterian Laboratory of Experimental Medicine and the Department of Pharmacology, Johns Hopkins University.)

It has always been a difficult matter to cut an accurate opening between the portal vein and vena cava once they have been united side to side. Almost equally difficult has it been to control hemorrhage following the above procedure.

We communicated the method of doing this operation (Eck's fistula), not long ago, which gave excellent results in our own hands. The actual cutting of the fistula was fraught with a certain amount of danger because we used only an ordinary small eye-scissors. The control of bleeding following the cut, however, was beautifully and absolutely done by the mattress suture we suggested.

In order to do away with practically all danger in cutting the opening, we have lately devised a pair of scissors (Figs. 1 and 2), that are mathematical in the precision in which they cut and yet are so simple in their mechanism that any one can use them with perfect success. They are bayonet shaped, so that there is no difficulty or awkwardness in approaching the vessels which naturally lie quite deeply. The handles are four inches long, with a one and a half inch drop to the blades, whose actual cutting edge is 1 cm. There are two separate "stops," which allow the blades to be opened only a certain distance. When they are opened to their fullest extent, their points are exactly one-quarter of an inch apart and their outer edges are almost parallel—as nearly parallel as an instrument maker can make them and still keep the inner edge for cutting purposes. Furthermore the blades are wedge shaped, so as to prevent all bleeding while entering the vessels. Raised above the blades one-quarter of an inch and running parallel to them is a round guide which projects out beyond the blade points one-half inch and is turned up at its ends. It is attached to the shank of the scissors.

In addition to this improvement in our operation, the method of using which will be given a little later, we wish to tell of another aid which at first sight seems rather trivial, but is really of considerable significance and of great help. Where formerly we used single thread (Brainerd & Armstrong, size A or B), we now use double, threaded on the usual curved No. 3 French needle. The reason for this is that the double thread almost entirely fills the needle holes and is, of course, stronger.

The silk penetrates the lumen of both vessels at every stitch, but such a thing as a thrombus is practically unknown in this work. We remarked upon this phenomenon in our first paper, but were unable to explain it. A number of observations have been made since then, but no satisfactory explanation has been forthcoming.[1]

The steps of the operation then, as now done, are as follows:

A dog of almost any size, male or female, is kept on a restricted diet for about forty-eight hours to insure an empty intestinal canal. Having then been prepared for operation in the usual manner, the animal is etherized and the abdomen is opened in the mid-line in females, through the right rectus in males. With the intestines packed off to the left,[2] the portal vein and vena cava will be found lying very close to each other and running parallel for a considerable distance.

A provisional ligature of heavy silk is then placed around the portal vein in the space between its bifurcation at the hilus of the liver and the entrance into it of the vena pancreatico-duodenalis. This ligature, of course, is not tied until the conclusion of the anastomosis.

Following this, by blunt dissection the portal vein is cleared of peritoneum and all superfluous fat for a space of about an inch and a half. It is unnecessary to disturb the vena cava at all.

The left side of the vena cava is now united to the adjacent side of the portal vein, for a distance of about one inch (Fig. 3), by a continuous suture of double silk (Brainerd & Armstrong, size A), threated on a curved No. 3 French needle. The needle is passed through all the coats of both vessels, very little hemorrhage occurs, because the thread is of such size that it almost completely fills the needle holes. The slight bleeding which does take place is accurately controlled by gentle traction on the stitch previously placed. The suture is

[1] To those who are familiar with the delicacy of the manipulations necessary to the success of a blood vessel anastomosis elsewhere in the body, this phenomenon is a most extraordinary occurrence. Thrombus formation in doing transfusion and arterio-venous anastomosis, or even a repair of a wounded vessel is the one thing that is to be most greatly feared by the surgeon, and all sorts of precautions are taken to avoid it. Yet here it seems that no precautions whatsoever are necessary because it almost never occurs, if the following precautions are taken. The animal should be put on a diet poor in calcium salts (meat) for several days previous to the operation and starved for 24 hours.

[2] It is of the utmost importance to leave the intestines in the abdominal cavity, so as to prevent any tension on the portal vein and consequently the tearing out of a stitch. The mattress suture especially is liable to cut out of the portal vein, if this precaution is not taken.

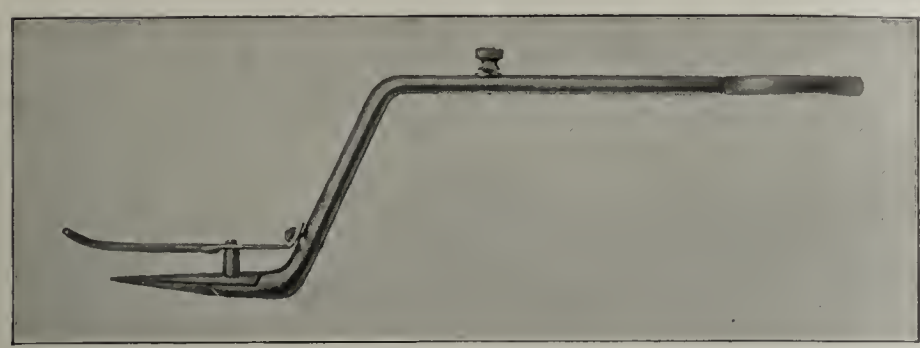

Fig. 1

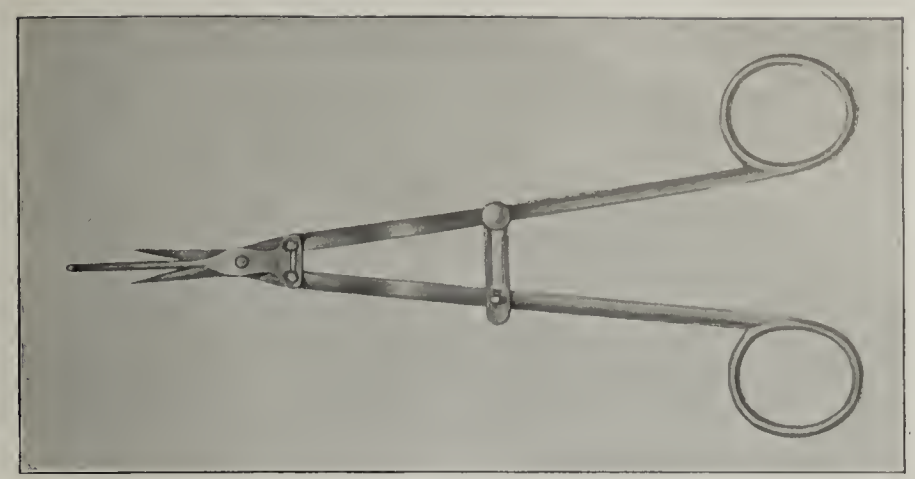

Fig. 2

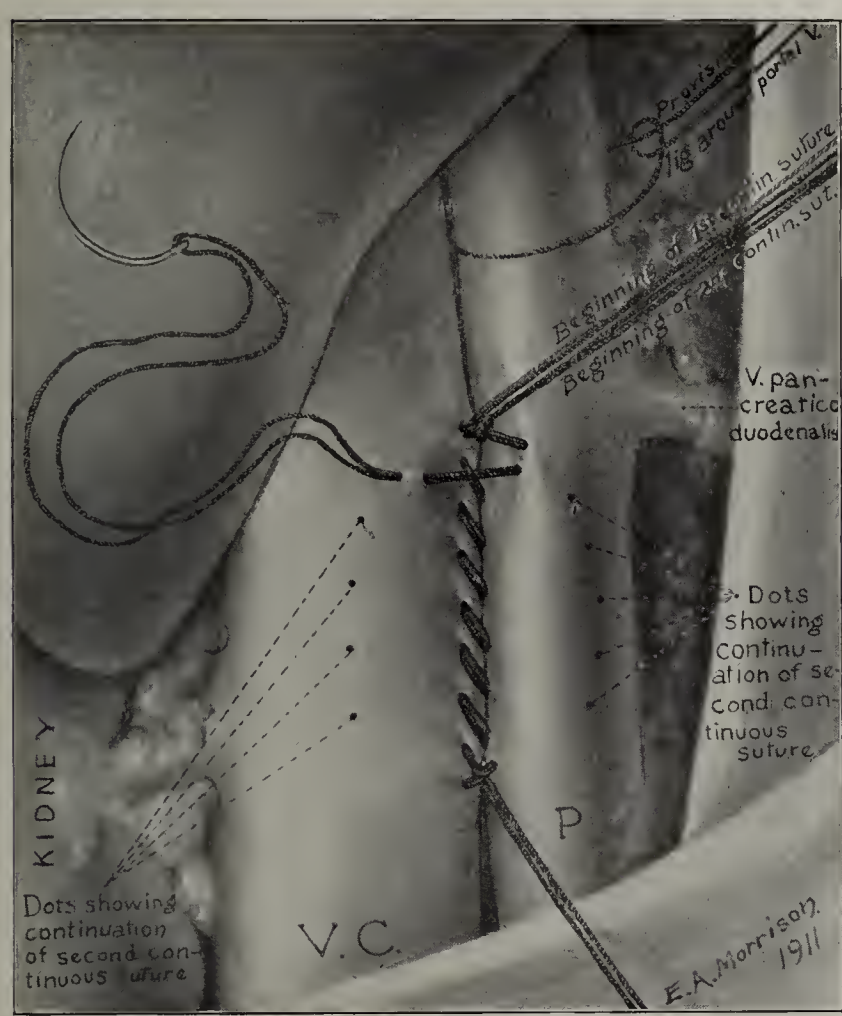

Fig. 3

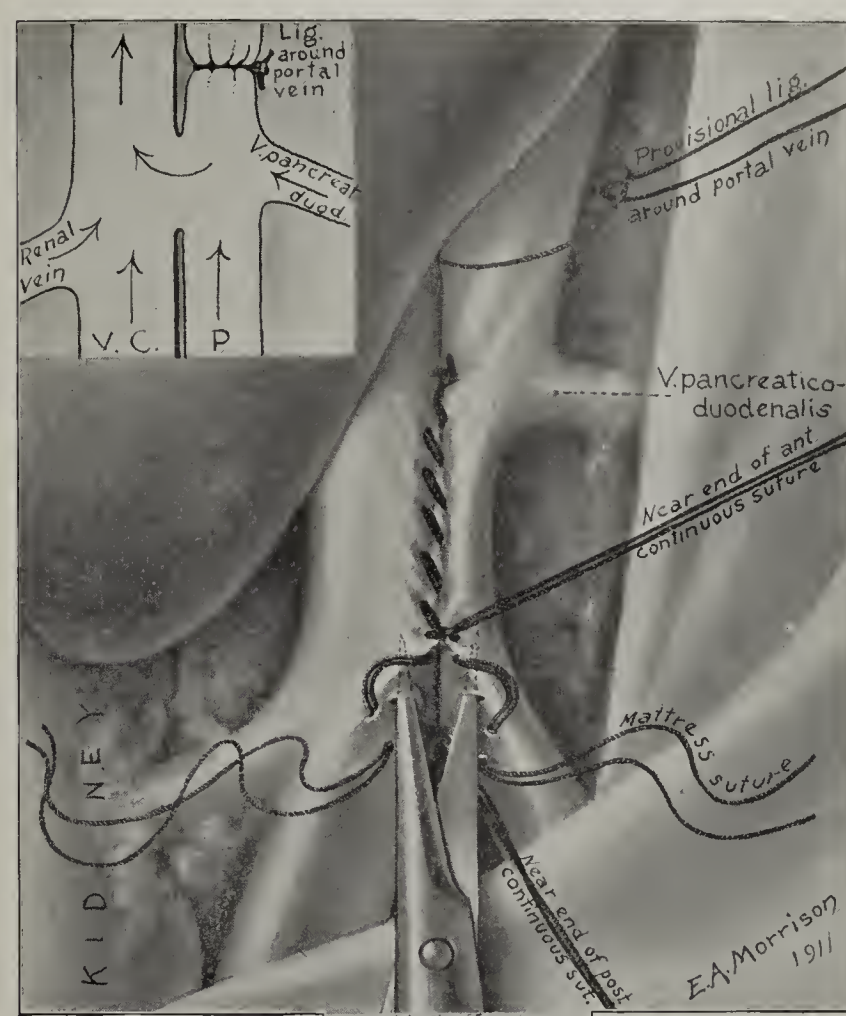

Fig. 4

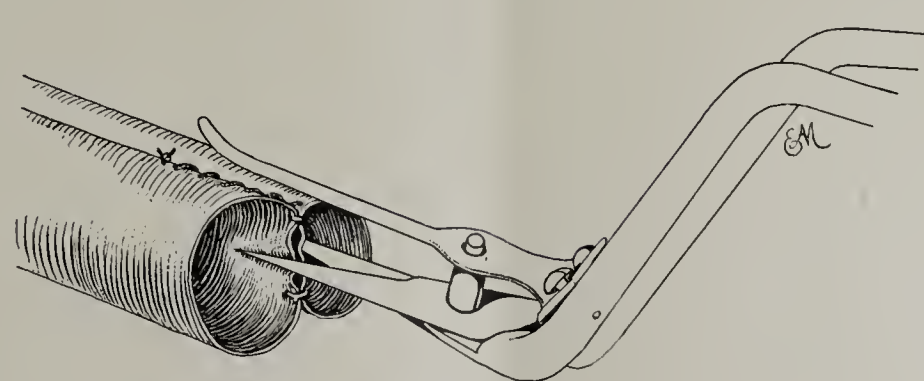

Fig. 5

started above and continued downwards, the ends being left long to be subsequently made use of as tractors.

Starting again at the top with another suture, just as in making a lateral anastomosis of the intestines, the portal vein is made to overlap the vena cava. This suture, also a continuous one, is brought down the outer sides of the vena cava and portal veins, parallel with the first suture—as indicated in the dots in Fig. 3—for a distance of about three-quarters of an inch, when it is tied, the ends being left long.

In the space between the lower ends of the two continuous sutures, a mattress suture is placed, having one arm in the portal vein and one in the vena cava (Fig. 4). Between the arms of this suture, which is left loose and untied the blades of the Eck fistula scissors are passed into the vessels, one entering the lumen of the portal and the other that of the vena cava. If now upward traction (that is at right angles to the vessels) is put upon the near end of the anterior continuous suture, and if the guide which is, of course outside the vessels is kept absolutely parallel to the upper row of sutures, the blades, being opened to their fullest extent, can be sent into the vessels up to the hilt (Fig. 5), without the slightest danger of cutting the upper or lower rows of sutures or of puncturing either vessel laterally. A cut exactly 1 cm. long is then deliberately made, and the scissors withdrawn, the forefinger of the operator or assistant being slipped over the external hole made in the vessel by the scissors and held there while the mattress suture, also of double silk, is tied. If this suture has been properly placed the hemorrhage will be accurately controlled. The ends of the mattress suture may be tied to the ends of the continuous sutures if additional security is desired, though this precaution is rarely necessary.

The anastomosis having thus been completed, the ligature, placed at the beginning of the operation around the portal vein at the hilus of the liver, is tied. The abdomen is then closed in layers, and following the usual custom of the Hunterian laboratory the wound is left without a dressing.

Since making use of the above mentioned scissors, we have not had a single fatality attributable to them, although we have done this operation in over 25 animals. About the only accidents we now have are those due to the misplacing of a stitch, the tearing out of a stitch or to some similar misfortune encountered during the actual anastomosis of the vessel, most of which, however, can be avoided by careful work.

I. Effect of Diet on General Behavior of Eck Fistula Dogs.

It was Eck's original intention to use his operation in the treatment of certain pathological conditions (especially abdominal ascites, due to cirrhosis of the liver). His method, however, was so unsafe that he did not venture to perform the operation on human beings. The well known researches of Pawlow and Nencki and their collaborators resulted in a great improvement of the tecnic of the operation, but at the same time it was found that animals (dogs), with an Eck fistula, if put on an exclusive meat diet, behaved quite differently from normal ones, in that they developed acute ammonium poisoning. These authors therefore concluded, that the liver normally takes care of and detoxifies the ammonium salts formed in the process of intestinal protein digestion. In the case of the Eck fistula animal the ammonium salts reach the general circulation and produce their typical toxic effects, before passing to the liver by way of the hepatic artery. As was natural, the likelihood of such an intoxication made the application of the Eck fistula operation to human beings an impossibility.

Hawk in a more recent research observed that beef extract (Liebig's) proved very injurious to Eck fistula dogs, whereas meat deprived of its extractives seemed to be harmless. To what constituent of the meat extract this toxic action is due, we are unable to say. From studies by Towles and Voegtlin, it seems that creatin, the most prominent organic constituent of meat extract, cannot play any rôle in this intoxication. Eck fistula dogs if kept on a diet of milk, though usually losing weight, will live for months as stated by many observers. In our own series of experiments (over 100 animals), we had an opportunity to confirm the statements of the Russian physiologists concerning the injurious effects of a pure meat diet.

We have made, however, the following observations. A great number of our Eck fistula animals, fed during several months on a meat diet to which bones had been added did not show any evidence of intoxication. We are unable to offer an entirely satisfactory explanation for this observation, unless we assume that the calcium phosphate of bone had some retarding influence on the rate of digestion, and consequently on the absorption of ammonium salts from the intestinal canal. The antagonistic action of calcium to ammonium salts, as observed by King and Voegtlin, may also have been the deciding factor in preventing the intoxication.[3]

We furthermore found, that on a mixed diet, consisting of milk, meat and bread, these dogs will live for a long time without showing any noticeable abnormalities. They gain in weight and are lively in appearance. The sexual functions are not impaired. The urine does not contain any abnormal constituents. We have kept several of these animals alive for more than ten months.

A careful study of the various hepatic functions in Eck fistula dogs disclosed the fact that although no qualitative changes could be determined, certain metabolic processes were found to be more or less depressed.

II. Carbohydrate Metabolism in Eck Fistula Dogs.

Popelski states that Eck fistula dogs show a lowered tolerance for glucose, *i. e.* alimentary glycosuria appears more readily if sugar is fed to such animals. de Filippi in a splendid research carefully studied this question in especial relation to the theory of Claude Bernard on the glycogenetic function of the liver. As is well known Bernard reached the conclusion that during digestion it is the liver which takes up all the sugar

[3] The intravenous injection of calcium chloride during the height of the intoxication did not exhibit any curative action. Guthrie states that he was unable to produce a toxæmia in Eck fistula cats by means of a meat diet.

brought to it by the portal circulation, that glycogen is formed and is mostly deposited in the liver cells, and is given up to other organs as they require it. Great stress has been laid on this function of the liver. It is the general belief that the liver is the regulating organ of carbohydrate metabolism, and that it prevents the accumulation of sugar in the blood (hyperglycæmia) and the appearance of sugar in the urine. It was de Filippi who was the first to call attention to the fact that an Eck fistula animal does not exhibit severe changes in carbohydrate metabolism; although its liver is practically excluded from the circulation (since the hepatic artery brings only a relatively small amount of blood to this organ). The sugar tolerance is only slightly decreased. This author therefore concludes that other organs may compensate the loss of liver function in regard to glycogenesis. He actually was able to demonstrate that the muscles of Eck fistula dogs in some cases contained more glycogen than those of normal control animals.

In our experience we could confirm the view expressed by de Filippi. With the exception of a few animals which were fed on large amounts of milk (800 cc. to dogs weighing 8 kgs.), no sugar could be detected in the urine. It seems, however, that lactose, levulose, saccharose, and glucose are less utilized by the Eck fistula dog, if introduced in relatively large quantities. These observations are important in connection with the clinical test for liver function described by H. Strauss and a few remarks as to the value of this test may not be superfluous. Strauss had observed that frogs with their livers extirpated showed a reduced tolerance for levulose. He therefore made use of this hexose to test hepatic function of patients with liver diseases. The results obtained seemed at first to indicate that the test was of some value, but later observers did not altogether corroborate the findings of Strauss. We believe that observations made on the frog, an animal so far removed from the human, cannot with any reason be transferred to the latter. From the work of de Filippi and our own observations on mammals, we are inclined to think that such a test could hardly prove successful, as there are great individual variations in the sugar tolerance, and also because a great reduction in liver tissue—three quarters—can take place before any abnormalities occur.

III. Bile Formation and Hemolytic Function of the Liver in Eck Fistula Dogs.

In a recent article, we have been able to prove the interesting fact that the formation of bile pigments and bile acids is very markedly decreased in the Eck fistula dog. The depression of this liver function occurs to such an extent that ligation of the common bile duct is not followed by obstructive jaundice, and only a negligible excretion of bile pigments and bile acids in the urine. We were led to believe from certain histological observations in connection with our work that some of the red blood corpuscles passing through the liver are taken up by the cells of this organ and are broken down, thus liberating hemoglobin. The latter substance gives rise to the formation of bile pigments. According to our experiments, the amount of bile pigments formed is dependent on the blood flow through the liver. In the case of the Eck fistula animal much less blood passes the capillary system of this organ and therefore fewer red blood corpuscles are brought into contact with the liver cells. It seems plausible that under these conditions a smaller number of erythrocytes are broken up. It may be emphasized that this reasoning is based on indirect evidence. The histologic picture of the livers of some of our animals showed that this organ was in a state of atrophy, which is explained by Whipple and Sperry by the insufficient blood supply of the liver cells under these conditions.

Dr. S. A. Matthews kindly informed us that he was able to corroborate these results on bile formation in every detail, and that he had direct proof of the remarkable decrease in bile formation after the operation for an Eck fistula, in that the flow of bile from a biliary fistula decreased very much up to practically complete cessation.

As a direct result of the reduction in bile secretion the feces of Eck fistula dogs on a milk diet appear fatty, whereas normal controls do not excrete any fat under these conditions. We are studying this point quantitatively at the present time.

Many interesting questions can be raised in regard to the fate of other bile constituents such as cholesterin, which as far as we know, is eliminated from the body with the bile and is transformed to dihydrocholesterin in the intestines and appears in the feces as such in relatively large amounts. In one of our Eck fistula dogs in which the common bile duct had been resected and which lived for more than ten months the path of excretion for cholesterin, namely, the bile duct, was blocked and yet the presence of this substance could not be demonstrated in the urine, nor in the feces. It seems to be especially worth while to consider this question, as we know that cholesterin plays an important part in certain immunity reactions (hemolysis by cobra venom). The recent work of Abel and Macht has demonstrated the most powerful digitalis action of an oxydative product of cholesterin found in the venom of the tropical toad *Bufo agua*. We hope to take up in the near future a study of the relation of cholesterin to hepatic function.

Clinical Application.

That the danger of intoxication by errors in diet is remote in the human being with an occluded portal circulation is shown by the following case reported by Schulz and Müller: These observers describe a patient with thrombosis of the portal vein near the liver hilus, in which there was complete obstruction. The patient came to the clinic suffering from severe ascites, but otherwise in good condition. The fluid was removed every two weeks during a year. The nutritional condition was perfectly normal, as shown by the weight. Superficial compensatory circulation was fully established. At autopsy no anastomosing vessels were found between the portal system and the liver.

At a recent session of the German Surgical Society, Bier reported that he had opened the abdomen of two patients suffering from cirrhosis of the liver with a view to anastomosing the portal vein, and the vena cava. In both instances the ad-

hesions were so dense around the hilus of the liver that the attempt had to be given up. Notwithstanding this, Bier, said, that when he got what he considered to be another suitable patient, he would try again to do an Eck fistula. Several surgeons, especially Vidal in France, and some in Italy, have had experiences similar to those of Bier. Indeed Vidal did actually perform the operation only to lose the patient three months later from an infection.

That the portal vein and vena cava will actually be successfully anastomosed in human beings in the near future is our firm conviction. The feasibility of the operation is beyond question. We have proved, we believe, that life is perfectly compatible with such a condition. In those suffering from cirrhosis of the liver, we believe, that an Eck fistula will give the relief that has been earnestly desired. It is only necessary to obtain a patient early enough in the course of the disease to carry out the various steps of the procedure. In such an individual the operation will be more easily performed than in the dog.

Summary.

1. A new modification of the operation for Eck fistula is described which is superior as far as safety is concerned to the methods already known.

2. Eck fistula dogs if kept on a proper diet may live without being influenced by the operation for a long time.

3. Certain hepatic functions are decreased in Eck fistula animals: tolerance for sugars, formation of bile, hemolytic function of the liver.

4. Proof is furnished for the assumption that the application of the operation to the human being is perfectly compatible with life.

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SOME SUGGESTIONS REGARDING THE MECHANISM OF RESORPTION OF THYROID COLLOID.*

By Paul G. Woolley, M. D., Cincinnati, O.

If one examines the recent literature on the physiologic relation of the thyroid to the general economy, one finds that while there is some histologic evidence of resorption of the characteristic colloid, and much physiologic evidence of the same process, yet there is no, or practically no, reasonable explanation offered as to the method by which this resorption is accomplished. Thus, Hirsch[1] remarks that there is no doubt that a part of the product of the thyroid gland enters the circulation, *but that the method by which the colloidal contents of the follicles reach the lymph-spaces or blood-vessels is not yet known.*

In Hirsch's article the concept of Hürthle is quoted to the effect that the colloidal material enters the lymphatic circulation by means of intercellular passageways which unite the follicles with the general lymphatic system. This statement would lead to the embryologic conception that in reality the follicles are lymphatic, or to a histologic conception which has not yet been substantiated and which would mean that in the thyroid there is an anatomical arrangement which is contrary to the general rule that holds in all other organs. But whether this idea or the one that supposes the necessity for an *Einschmelzung* of the epithelium which allows of a breaking through of the colloid masses into the lymph-spaces is true or false, the ultimate proposition is helped not at all, for even in the lymph-spaces the colloid must be changed in order that it may be available for other cells, and for passage through the walls of the smallest capillaries. It would be of little importance, in the long run, whether this change occurred in the follicles of the thyroid or in the lymph-spaces or blood-vessels, and since there is no anatomical evidence of the colloid passing the follicle walls in the condition in which it exists in the follicles, it seems most reasonable to suspect that the necessary change in structure occurs within the follicles.

The substance which morphologists call the thyroid *colloid* is correctly so-called if we consider it from the standpoint of physico-chemical behavior. It is gelatinous, viscid and non-diffusible. It is this character of non-diffusibility which concerns us at this time, for were the thyroid colloid to remain non-diffusible, then it could have no physiologic value. But such colloid substances may be converted by various methods into the crystalloidal state without sacrificing their purely chemical nature. When they are so converted they become more fluid, non-viscid, and diffusible. Such a change, I believe, explains the migration of thyroid colloid material into the blood and lymph streams and from there into the various tissues and cells of the body.

*Read before the Cincinnati Society of Medical Research, October 5, 1911.

[1] Handbuch d. Biochemie d. Menschen u. d. Tiere, Bd. III, Hft. 1, S. 273.

As an example of reversibility in the state of a substance, I may merely mention the melting of gelatine, agar, or glue by the application of heat, and the transformation of glycogen into dextrose (accompanied in this case by the addition of a molecule of water to the carbohydrate molecule).

Substances brought to the thyroid by the blood stream in a diffusible condition are stored in a colloid state in the follicles, and later, when necessity arises or when, in disease, the chemical conditions are right, there follows a change that results in a transformation from the colloid to the crystalloidal state. By such a supposition we can dispense with theoretical anatomical variations, and can, most important of all, have at our disposal a working hypothesis that can be tested. We might therefore suspect that the præcolloid of Lewandowsky is the crystalloidal state of follicular colloid.

It might be suggested that in the process of resorption of the thyroid colloid we are dealing with an instance of the diffusion of a colloid through a colloid—of the passage of the thyroid colloid through the colloid walls of the follicles. But in this case we have no evidence of such a process. Certainly we see colloid in the alveoli, in the epithelial cells and in the lymph-spaces. But the colloid masses of the cells are evidently in the process of extension into the alveoli and are not, apparently, on the road to the exterior. In the case of the colloid in the lymph-spaces we are possibly dealing with a reversion, to the colloid state, of material that has entered these spaces in crystalloidal form, and which, because of an overabundant diffusion and consequent chemical changes resulting from an already sufficient supply of thyroid secretion in the organism, has been changed again to the colloid state.

In the structure of goiters we have certain indications of the truth of this hypothesis. A colloid goiter, composed of large alveoli filled with well-formed colloid, gives no symptoms unless these be on the hypothyroidism side of the picture. But suppose we massage such a goiter, increase the blood supply to it, and therefore increase the activity of the cells? Then, in certain cases at least, we may produce the opposite picture of hyperthyroidism, due theoretically to increased resorption of colloid.

In exophthalmic goiter, on the other hand, in which there is the symptom-complex of hyperthyroidism, and the anatomic picture of cellular activity, the alveoli are small and such colloid as is present shows none of the density of normal thyroid colloid. The whole physiologic and anatomic picture points perhaps not to resorption of colloid, but, at least, to an absence of the typical colloid state, if it be not the retention of the crystalloid state or one closely allied thereto. Certainly the cells of exophthalmic goiters are more actively functioning than those of colloid goiters. But it is true that they are active in an abnormal way, because they produce a secretion that does not undergo the normal change into the colloid state. Theoretically the cells themselves may produce, under abnormal conditions, substances which prevent colloidal transformation or the blood stream may bring from other abnormally functioning organs materials that prevent the normal change, so that the colloid, instead of being stored in the acini, is constantly resorbed and the cells of the thyroid are thereby stimulated to increased production.

There are therefore two points of view to be considered in the physiology of goiter; one, that the cells produce a normal secretion that is modified by outside influences; the other that the cells are abnormal in their activities. There is evidence that both are true, and theoretically both may be active in the same way; namely, by influencing the physical character of the colloid.

It was with the idea of testing, roughly at first, whether thyroid colloid (iodine-containing colloid) could be influenced by certain external influences, that the following experiments were made. The very simple methods employed in physico-chemical studies of the colloidal state were used.

Cubes of fresh hog thyroid weighing 1 gram were immersed in dilute solutions of acids and physiologic salt solution for twenty-four hours. $\frac{N.}{200}$ sulphuric, nitric, hydrochloric, acetic, lactic, tartaric and formic acids were used. At the end of twenty-four hours the fluid in which the tissue had been immersed was filtered and the filtrate was boiled on a water bath. The coagula produced by boiling were collected on filter papers, washed, dried, fused, oxidized and finally titrated with $Na_2S_2O_3$, following the method of Hunter.[2] The fresh thyroid contained an average of about 0.3% iodine when treated by this method.

The results of the several experiments were as follows: Using lactic acid, no coagulum was produced by boiling. The coagulum from the tartaric acid tube contained 0.00005 gm. I; from the formic acid, 0.0001 gm. I; from the acetic acid, 0.00028 gm. I; from the sulphuric acid, 0.0004 gm. I; from the nitric acid, 0.00018 gm. I; the hydrochloric acid residue was lost.

These results, rough though they be, are interesting and suggestive, especially if one compares them with Martin Fischer's experiments on the effects of acids on the swelling of (protein) colloids. Fischer, using $\frac{N.}{20}$ acids, found that hydrochloric acid produced the greatest effect in twenty-four hours, and that it was followed by HNO_3, H_2SO_4 and $HC_2H_3O_2$, in the order given. Applying Fischer's conclusions, there is the indication that the changes in the diffusibility or "solution" of the colloid of the thyroid gland is intimately associated with the physico-chemical conditions surrounding it, and that these changes seem to be comparable to those taking place in the kidney in edema and nephritis.[3] If further experiments justify this conception, therapeutic possibilities will at once suggest themselves, and will form the subject of discussion. In the meantime it is my intention to make further experiments to determine the actual differences in diffusibility of thyroid colloid by means of membranes.

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[2] Chem. Centralbl., 1910, XI, 760.

[3] Oedema. New York, 1910, John Wiley & Sons. Das Oedem. Dresden, 1910, Th. Steinkopf.

THE INFLUENCE OF FEEDING IODIDES ON THE CATALYTIC ACTIVITY OF THE RABBIT'S BLOOD.

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Studying the influence of sodium arsenite on the catalytic activity of the rabbit's blood, Duncker and Jodlbauer [1] found that in non-toxic doses this substance increases the power of the blood to decompose hydrogen peroxide in poorly nourished animals. In a series of experiments on rabbits it was found that the administration of potassium or sodium iodide *per os* may lead to an increase of the catalytic activity of the blood of these animals. The technique determining the catalytic activity of the blood was the one used by Kastle and Loevenhart [2], adapted to the purpose as in the investigations of Winternitz.[3] The figures recorded designate the number of cubic centimeters of oxygen liberated in one minute. This is sufficient, although readings were taken every fifteen seconds and frequently for two minutes. With very few exceptions duplicate determinations were carried out and the figures represent the averages of two well-agreeing determinations, the differences not exceeding two cubic centimeters. To eliminate the possibility of a simple salt action a few control experiments were made with sodium chloride. It was the intention to administer the iodide on an empty stomach, but it became evident that the withholding of food is not without an influence on the catalytic activity of the blood. The accompanying Table I registers the days of observation from the beginning of the experiments. Where several observations were made on the same day the hours elapsed after the administration of the drug are recorded. The substance administered and its dose are given. In the starvation experiments, where the animals received only water, the beginning and end are noted; the weight of the animals in grams is added.

In some cases only one observation preceded the administration of the drug. This was deemed sufficient, since according to Winternitz [4] the catalytic activity of the blood of the same rabbit remains nearly constant. No. V really gave nearly constant results, but Nos. IV and XI showed larger variations, which do not seem to be uncommon. The results obtained with the administration of the iodine salts may be briefly summarized as follows:

TABLE II.

Dose of Iodide per Kilo.	No. of Animals.
0.0–1.1 gm.	V(1)o, V(2)o, VIII(1), VIII(2)o
1.6–2.0 gm.	V(3)+? VII(3)+? VIII(3)+, X(3)+, XI(2)o, XII(3)+
2.0–3.0 gm.	I(5)+, II(5)+, III(5)+, IV(4)+, V(4)o, VI(5)+, X(4)+?
3.0–4.0 gm. and over	IV(5)+, IV(6)+, V(5)+, V(6)+, XI(5)+, XII(4)o

Here the dosage in grams is given in parenthesis corresponding to the dosage given in Table I. Wherever a rise of the catalytic activity occurred, whether only transitory or more lasting, a plus sign is affixed, while an "o" signifies that a rise did not occur. It is uncertain whether the rise in No. X(4) with 2-3 gm. per kilo can be attributed to the drug, since the activity on the day of the administration had increased considerably above that noted two days previously. The second day following the administration of the drug the animal died, and at the autopsy a pneumonia was found. The same lesions were found in No. VII, dying on the third day after receiving sodium iodide. In this case no very definite increase of the catalytic activity was noted. Winternitz, Henry and McPhedran [3] state that the catalytic activity of the blood is not increased in pneumonia. Although animal No. X had shown a definite increase in the catalytic activity of its blood in a previous experiment with 1.6-2.0 gm. iodide per kilo, the conditions of this last experiment make it very possible that some other factor besides the administration of the drug played a rôle in the subsequent increase of the catalytic activity.

A glance at Table II shows that a dosage of about 1 gm. iodide per kilo has no effect on the catalytic activity of the blood. With ½ gm. per kilo the effect was uncertain, being decided in Nos. VIII, X and XII, negative in No. XI and doubtful in Nos. V and VII. With 2-3 gm. per kilo the effect was negative in No. V, positive in Nos. I, II, III, IV and VI. With 3 gm. per kilo and over the effect was positive in IV, V and XI, negative in XII. In this latter case it must be remarked that the animal had lost considerable weight after having previously reacted positively to a smaller dose.

Some of the animals, as noted in Table I, died during the administration of the drug or immediately after, without showing any pronounced lesions.

As may be seen from Table I, in several instances the rise of the catalytic activity was only transitory, being limited to the day of the administration of the drug; in others the maximum was reached from the second to the fourth day.

It may be noted that the catalytic activity of the blood of animals observed for a longer period of time, and subjected to a number of experiments like Nos. IV, V and XI, seemed to assume gradually a lower level, perhaps with a tendency to greater oscillations.

The iodides were always given in enough water to make a 4 per cent solution. The sodium chloride in Nos. IV and XI was given in the same dilution. In both these cases the administration of this salt had no effect, while both reacted to the administration of iodide.

The starvation experiments in Nos. II, IV, V and XI showed, with exception of No. IV, some increase of the catalytic activity while in each case a more or less pronounced decrease occurred with the resumption of feeding.

TABLE I.

I.	Wt. 2,270 g.		1 hr.	4½ hr.	6 hr.	2 d.	3 d.	4 d.							Remarks.
	1 d.	5 g KI													
5 g KI.	39.0		41.0	42.5	41.0	44.5	46.5	Dead							No autopsy.
II.	Wt. 2,200 g.		1 hr.	4½ hr.	6 hr.	2 d.	3 d.	4 d.	5 d.	7 d.	8 d.	10 d.	Starved		Died before administration of KI was finished. Stomach tube *in situ proprio.* No lesions of stomach. Œdema of lung.
	1 d.	5 g KI													
5 g KI. Starvation.	32.5		36.0	38.0	37.5	41.5	40.5	41.0	44.0	36.0	37.0	36			
	11 d.	12 d.	Fed	13 d.	14 d.	15 d.	16 d.	17 d.	18 d.	19 d.	21 d.	26 d.	1 g KI.		
	38.0	40.0		38.0	33.5	36.0	36.0	34.0	31.0	29.5	28.0	33.5	Died		
III.	1 d.	2 d.	3 d.	4 d.	5 d.	Wt. 2,150 g.		5 g KI.	9 d.	10 d.					
						6 d.	8 d.								
5 g KI.	36.4	36.5	36.5	35.5	37.0	38.4	35.7		46.0	Died					No autopsy.
IV.	1 d.	3 d.	4 d.	5 d.	8 d.	5 g NaCl.	3 hr.	5 hr.	9 d.	10 d.	11 d.	12 d.	Wt. 1,600 g.		Marked diarrhœa on 22d, 23d, 32d, and 33d days. Autopsy showed congestion and small hæmorrhages in lungs. In stomach, area of congestion about the size of a silver dollar.
													13 d.	15 d.	
5 g NaCl. 4 g KI. Starvation. 5 g KI. 6 g KI.	27.0	28.4	28.9	27.4	23.8		24.9	23.7	25.2	24.4	24.1	23.7	22.9	23.2	
	4 g KI.	3 hr.	5 hr.	16 d.	17 d.	18 d.	Starved	19 d.	20 d.	Fed	22 d.	5 g KI.	3 hr.	5 hr.	
		27.8	25.3	23.9	24.7	23.7		23.6	24.5		17.9		24.7	24.0	
	23 d.	24 d.	25 d.	26 d.	27 d.	28 d.	Wt. 1,300 g.		3 hr.	33 d.	34 d.				
							32 d.	6 g KI.							
	18.6	14.8	19.0	15.5	16.7	15.1	18.1		23.5	19.8	Died				
V.	1 d.	2 d.	3 d.	4 d.	5 d.	Wt. 1,870 g.		1 g KI.	9 d.	10 d.	1 g KI.	11 d.	1 g KI.	12 d.	Marked diarrhœa on 36th, 37th, 46th, and 47th days.
						6 d.	8 d.								
1 g KI. 2 g KI. 3 g KI. 3 g NaI. 4 g KI. Starvation. 5 g KI. 6 g KI. Starvation.	30.4	32.2	30.0	30.0	30.8	30.5	31.3		28.1	30.1		29.3		29.8	
	2 g KI.	13 d.	2 g KI.	14 d.	3 g KI.	15 d.	17 d.	18 d.	3 g NaI.	2½ hr.	4½ hr.	19 d.	20 d.	22 d.	
		28.5		29.4		31.2	32.6	32.6		34.3	30.7	29.1	27.3	28.3	
	25 d.	Wt. 1,700 g.		4 g KI.	3 hr.	5 hr.	30 d.	31 d.	32 d.	Starved	33 d.	34 d.	Fed	36 d.	
		26 d.	29 d.												
	25.6	26.8	25.0		25.6	26.2	23.7	25.3	23.7		26.5	26.5		21.6	
	5 g KI.	3 hr.	5 hr.	37 d.	38 d.	39 d.	40 d.	41 d.	Wt. 1,500 g.		6 g KI.	3 hr.	47 d.	48 d.	
									42 d.	46 d.					
		27.4	26.1	18.8	16.7	18.6	14.9	18.3	14.2	18.0		21.9	20.6	18.1	
	49 d.	Starved	50 d.	Wt. 1,180 g.		Fed	Wt. 1,230 g.		56 d.	58 d.					
				51 d.	52 d.		53 d.	54 d.							
			20.3	22.4	22.5		18.0	20.0	20.6	18.3					
VI.	Wt. 1,850 g.		1½ hr.	5 hr.	2 d.	3 d.									Œdema and extensive hæmorrhages in lungs. In mucosa of stomach two old superficial ulcers without signs of active inflammation.
	1 d.	5 g NaI													
5 g NaI.	30.4		34.3	34.8	31.0	Died									
VII.	Wt. 1,450 g.		3 hr.	5 hr.	2 d.	3 d.	4 d.								Appeared sick on third day, died on fourth. Pneumonia of right lung. Stomach normal.
	1 d.	3 g NaI													
3 g NaI.	26.6		28.3	29.4	27.8	28.0	Died								
VIII.	1 d.	Wt. 1,850 g.		1 g KI.	5 d.	6 d.	1 g KI.	7 d.	8 d.	2 g KI.	9 d.	2 g KI.	10 d.	2 g KI.	Died with first administration of 30 cc. 4 % KI solution. At autopsy no macroscopical lesions found.
		2 d.	4 d.												
1 g KI. 2 g KI.	35.8	35.2	33.6		32.7	33.9		32.1	33.7		32.8		31.0		
	11 d.	13 d.	14 d.	15 d.	16 d.	18 d.	21 d.	23 d.	25 d.	4 % KI.					
	31.7	34.0	34.8	36.0	35.7	35.6	35.3	33.0	33.3	Died					

TABLE I—*Continued.*

IX.	1 d.	2 d.	3 d.	4 d.	5 d.	6 d.	8 d.	5 g KI.							Died immediately after receiving KI. No macroscopical lesions found.
5 g KI.	30.3	32.6	32.4	32.5	30.4	29.9		Died.							
X.	1 d.	Wt. 1,880 g. 2 d.	Wt. 1,880 g. 4 d.	3 g KI.	4 d.	5 d.	6 d.	8 d.	Wt. 1,880 g. 9 d.	Wt. 1,880 g. 10 d.	11 d.	13 d.	4 g NaI	3 hr.	Pneumonia. In stomach a few congested areas.
3 g KI. 4 g NaI.	34.3	32.3	33.1		39.1	42.1	40.5	38	37.4	37.6	35.2	40.2		42.8	
	5 hr.	14 d.	15 d.												
	43.7	51.2	Died												
XI.	1 d.	2 d.	3 d.	Wt. 1,550 g. 4 d.	Wt. 1,550 g. 6 d.	5 g NaCl.	3 hr.	5 hr.	7 d.	8 d.	9 d.	11 d.	13 d.	Starved	Some diarrhœa on 33d day.
5 g NaCl. Starvation. 2 g KI. 5 g KI.	30.8	32.4	29.9	27.1	30.2		30.3	29.5	26.5	29.7	30.0	28.8			
	14 d.	15 d.	16 d.	Fed	17 d.	Wt. 1,250 g. 18 d.	Wt. 1,250 g. 19 d.	23 d.	2 g KI.	3 hr.	24 d.	2 g KI.	25 d.	2 g KI.	
	28.4	26.5	33.5		28.4	28.4	25.9	24.9		24.2	22.5		21.5		
	2 g KI. 26 d.	2 g KI. 27 d.	28 d.	29 d.	31 d.	33 d.	5 g KI.	Wt. 1,350 g. 3 hr.	Wt. 1,350 g. 34 d.	35 d.					
			22.5	24.0	21.9	22.8		30.3	24.4	20.8					
XII.	1 d.	Wt. 1,550 g. 2 d.	Wt. 1,550 g. 3 d.	3 g KI.	4 d.	6 d.	7 d.	8 d.	Wt. 1,100 g. 9 d.	Wt. 1,100 g. 11 d.	4 g NaI	3 hr.	5 hr.	12 d.	On 13th day it was difficult to obtain the necessary blood from the ear vessels of the emaciated rabbit. On 15th day the animal was very sick, refused food. Autopsy: No macroscopical lesions found.
3 g KI. 4 g NaI.	31.3	29.4	30.0		32.0	38.7	39.7	34.1	32.8	33.7		34.4	29.8	35.2	
	13 d.	14 d.	15 d.	17 d.											
	32.5	32.8	30.4	Died											

Wherever an increase of the catalytic activity occurred after the administration of iodide, this cannot be attributed to the presence of iodide as such in the blood. In the cases where the maximum was reached after two or four days the starch iodic acid test made with a few drops of blood had either diminished very considerably or was negative. Furthermore, a simple calculation shows that not sufficient iodide could have been present in the blood to account for the increase of the catalytic activity. Five cubic centimeters of a $\frac{N.}{100}$ solution of potassium iodide containing 0.0083 gm. KI liberated 0.5 cc. oxygen in sixty seconds from 5 cc. neutralized hydrogen peroxide. In all our experiments the Oakland dioxygen was used, containing about 3 per cent hydrogen peroxide. Supposing that the amount of blood of a rabbit is one twentieth of its body weight, a rabbit weighing 1000 gm. would have about 50 cc. blood. The amount of blood used in an experiment did not exceed 0.05 cc. This would be a thousandth part of the total blood. Let the dose of KI be 6 gm. and assume that all of this were present in the blood at one time, the amount of blood used would then contain a thousandth part of the dose, that is, 0.006 gm. KI, an amount insufficient to exercise an appreciable influence on the catalytic activity.

It is evident, therefore, that the rise of the catalytic activity of the blood following the administration of iodide must be due to an influence of the iodide on the organism. This influence manifests itself with any degree of constancy only after rather larger doses much exceeding the therapeutic doses, a reason why this investigation was not carried any farther.

CONCLUSIONS.

1. Potassium or sodium iodide fed to rabbits in large doses may lead to an increase of the catalytic activity of the blood.
2. This increase is not due to the presence of the iodide in the circulating blood.
3. Withholding the food may lead to an increase in the catalytic activity of the rabbit's blood, while resumption of feeding is associated with a drop, in its catalytic activity.

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4. Winternitz: The Catalytic Activity of the Blood, etc. J. Experim. M., 1909, XI, 200.

CONSANGUINEAL DIABETES MELLITUS.

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The occurrence of diabetes in several members of a family is relatively uncommon, but not so infrequent among those remotely related as it is in the case where brothers and sisters are afflicted with the disease. In the absence of exact knowledge of the etiology of the disorder, these instances in which one is tempted to consider some inherited defect as a cause are most interesting.* This is especially so in the case of children who suffer from diabetes. In the notable family, recorded by Charcot, with its four diabetic sons of a diabetic father, their occupation might be regarded as an etiological factor as they were all brewers, obese and gouty; but when diabetes manifests itself during the early years of life in several members of a family, one must consider also the possibility of some inherited factor as a probable cause.

Two families have come to my attention in which two or more children of the same parents have developed diabetes in early youth.

Family G.: † 1. J. G., aged 17, was found to have a low percentage of sugar in his urine on September 23, 1889. He had been in the habit of having his urine examined occasionally because his father had died of diabetes, and also a brother at the age of 18 and he was naturally a little anxious concerning himself. Sugar had not been found in this patient's urine previous to the above date and during the next nine years, from 1889 to 1898, no sugar was detected. In 1898 the urine again contained some glucose, always less than 1 per cent, for several weeks following a period of excessive use of alcohol; but this glycosuria was accompanied by none of the typical diabetic symptoms and disappeared quite promptly. This patient has remained well up to October, 1909.

2. The third son, E. G., a medical student, discovered accidentally, in 1897, that his urine contained sugar. At this time it was found that he was voiding an average of 120 ounces of urine per day but there were, at first, no pronounced symptoms noted by the patient other than a large volume of urine. On advice he dieted and thus reduced the volume of urine considerably. The 24 hour quantity of October 21, 1897, amounted to 53 ounces with 12 grains of sugar to the ounce (1590 cc. urine, 42 grams sugar). A short while after this he began to fail rapidly and by January 29, 1898, he had lost forty pounds in weight. Death occurred in the following month.

The second family, S., is not known to have any diabetic tendency in father, mother or grandparents. The father and mother are both strong, healthy people.

The first child, W. S., developed excessive thirst at the age of six years and on examination was found to have sugar in his urine. Up to this time he had been a healthy child having had only one sickness, measles. He died in coma one week after the onset of the symptoms.

The second child, F. S., developed his first symptoms at the age of eleven years and six months. He had excessive thirst and passed large amounts of sugar. He succumbed to his disease in six months after its onset.

The third child, L. S., was healthy until his seventeenth year when he began to have excessive thirst and an enormous appetite. Sugar in large amounts was constantly found in his urine up to his death which occurred about one year later.

R. S. had had no previous sickness, with the exception of scarlet fever, until the development of typical symptoms in his ninth year. This child came under my observation. He had lost several pounds in weight, had a fair appetite and excessive thirst. He voided on an average nearly two liters of urine per day and the sugar content ran as high as 10 per cent and was 100 grams on a restricted diet. He developed some cough and night sweats in the course of a few months and succumbed to the disease in coma.

In a careful perusal of the literature I have endeavored to collect all of the cases of diabetes occurring in brothers and sisters where the disease manifested itself in the early part of life. The following is a summary of the cases:

Richard Morton[1] reported four children of a family who became successively diabetic at the age of dentition. One of these survived at least four years.

Isenflamm[2] knew of seven children all of whom became diabetic on reaching the age of eight to nine years. The parents were healthy.

Marsh[3] "had heard of instances" in families where the disease was transmitted to the fourth generation.

Griessinger[4] found but three instances recorded in the literature of parents or fellow children having the disease.

Mosler[5] mentions a father and mother, both diabetic; two daughters both developed diabetes and a son of one of those daughters became diabetic also.

Bence Jones[6] has recorded two brothers and one sister, ranging in age from seven to fifteen years, who had diabetes.

Durand Fardel[7] has cited a family reported by W. Prout in which the disease manifested itself in three generations. The father was diabetic, and two of his children, son and daughter, became afflicted in adult life; a child of the woman developed diabetes before maturity.

Fardel[8] also mentions three brothers who consulted Thomas

* As an explanation of the degeneration of the islands of Langerhans in young diabetics Weichselbaum has suggested an hereditary defect which might render these structures more susceptible to toxic influences. Wien. klin. Wchnschr., 1911, XXIV, 153.

† I am indebted to my friend, Dr. Edward L. Keyes, Jr., for the complete history of this family.

[1] Opera medica. Amsterdam, 1696, I, VIII, 22-24.

[2] Versuch einiger praktischen Anmerkungen über die Eingeweide. Erlangen, 1784.

[3] Dublin Q. J. M. Sc., 1854, XVII, 17, footnote.

[4] Studien über Diabetes. Arch. f. physiol. Heilk., 1859, III, 16.

[5] Brit. M. J., 1864, VIII, 734.

[6] Med. Times and Gaz., 1865, XIV, 58.

[7] The reference to Prout's publication is not given by Fardel, and I have been unable to find this case in Prout's writings.

[8] Traité clinique et thérapeutique du diabète. Paris, 1869, 296.

Leigh for diabetes. The ages of the patients are not stated. Fardel had observed two families where there was a notable inherited predisposition. In one of these a man thirty-two years old had diabetes, and he had lost his father and a twenty-seven year old brother of the same disease. The other case was that of a woman of forty-seven years who had a severe type of the disorder. Her father, mother, and two of her sisters had died of diabetes, and her son, age fifteen, had sugar in his urine.

Seegen [9] summarizes his cases by stating that in ten instances the brother or sister was diabetic, while in four of these families the father or mother was diabetic and one or more children had died of the disease.

Schmitz [10] has recorded diabetes in two sisters, four and five years of age; the mother was also diabetic.

Rossbach [11] had charge of two diabetic children of a diabetic father.

Dickenson [12] quotes an oral communication of Thomas Watson, who had seen three children, two brothers and a sister, all with diabetes.

West [13] had charge of a girl three years old who had diabetes. Her brother and sister had died of the same disease at the age of two and two and a half years respectively.

Senator [14] knew of an instance of two brothers being affected, and also the family of a Polish Jew in which four children died of diabetes.

Frerichs [15] recorded the cases of a girl of twelve years and her brother, three years older. No reference is made to the parents.

Hertzka [16] knew of three sisters with the disease.

Roberts [17] knew of eight children in a family, all of whom became diabetic.

Pavy [18] mentions three children of the same parentage, two boys and a girl, who had diabetes; the father and mother were both healthy. In a second family the mother and grandmother were diabetic, while in the third generation there were four diabetic children. He refers also to the case of a woman who came to him for treatment for diabetes. She had lost a sister from diabetes at twenty-one years of age, and two brothers at twenty-eight and thirty-five years of age.

Flint,[19] in a summary, without references to the sources of his cases, reports diabetes in two sisters (two instances), another family where a brother and sister were affected and also two instances of two brothers being diabetic. The ages are not stated.

Auerbach [20] has referred to a remarkable family; the father had some form of psychosis, and the mother diabetes. There were eleven children, and of these five were mentally defective and two diabetic. In the third generation there were several cases of diabetes or psychosis.

Saundby [21] reported three sisters who became affected between the ages of eight and ten years.

Bieloousoff [22] has recorded a brother and sister with diabetes. The boy was fourteen and the girl five years old.

Wegeli [23] has observed a number of consanguineal instances of diabetes. In one family were two brothers; one died at 22 months and the other at 12 years of age. There was no diabetic ancestry, but the mother and grandmother suffered from migraine. In a second family the father was diabetic, and his two daughters, ages four and fourteen, developed the disease. The father was also diabetic in the third family, and two of his sons died of the disease at the ages of four and seven years. In the fourth family a girl of eleven became afflicted. She had lost a younger brother of diabetes, but the parents were healthy.

Von Noorden [24] has recorded a remarkable family, in several members of which diabetes developed in three generations. There were two children in the third generation.

Pleasants [25] reported two boys and two girls, in the fourth generation, in a diabetic family, similar to that reported by Von Noorden.

Haas [26] knew of a girl of nine years and her brother, aged five who were diabetic.

Gordon [27] has observed two sons, ages three and four years, of a diabetic mother. In these children diabetes was associated with myxœdema, and marked improvement followed the use of thyroid extract. The father was neurotic.

Rowell [28] reported a boy aged five and his sister, with diabetes. Naunyn [29] recorded the cases of two diabetic children, whose ancestry is not stated, but presumably of a non-diabetic family.

Langaker [30] recorded a family of eight children where parents and grandparents were healthy. Five brothers and sisters died of diabetes between the ages of four and eleven.

[9] Diabetes Mellitus. Leipzig, 1870, 62.
[10] Berl. klin. Wchnschr., 1873, X, 211.
[11] Berl. klin. Wchnschr., 1873, XI, 258.
[12] Diseases of the Kidneys and Urinary Derangements. London, 1875, 74.
[13] Diseases of Infancy and Childhood. London, 1875, 717.
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NOTES ON NEW BOOKS.

Modern Medicine: Its Theory and Practice in Original Contributions by American and Foreign Authors. Edited by William Osler, M. D., etc. Assisted by Thomas McCrae, M. D., etc. In Seven Volumes, Royal 8 vo. Illustrated. (*Philadelphia and New York: Lea and Febiger, 1907-1910.*)

The appearance of the last volume of Osler's Modern Medicine marks the culmination of a great editorial work. By far the most ambitious and successful collection of monographs ever attempted in the field of internal medicine on this Continent. In fact its only rival of importance in the English speaking world is Allbutt's System which has reappeared in a new and improved edition in England. A detailed comparison of the two would be out of place here, but we might say that the English System surpasses in presswork and style as its greater price justifies, but on the whole the American is more modern and better covers the field. The individual volumes have been reviewed in these pages with the exception of volume five and volume seven.

Volume five covers the Diseases of the Digestive Tract and contains a number of excellent chapters among those specially deserving notice are Riesman on the Diseases of the Mouth and Salivary Glands which brings together in considerable detail much that is scattered in the medical journals. Functional Diseases of the Stomach by Julius Friedenwald are also well described, with very full notes on treatment. Stengel's chapter on Diseases of the Intestines is very thorough and has excellent discussions of the pathology and bacteriology of the subject. Opie's handling of Diseases of the Pancreas is much the best in any system and the last chapter by A. O. J. Kelly, on the Diseases of the Liver, Gall-Bladder and Biliary Ducts, is only equalled in English by Rolleston's large work on the same subject. Altogether it is a most satisfactory and valuable addition to our literature.

The seventh volume, Diseases of the Nervous System, is a fitting climax to the series and contains an array of most excellent monographs. In the introductory paper of this volume, Barker discusses the senses and their symptomatology and presents in an unusually lucid manner the newer terminology and methods of investigators. Among the many excellent chapters, those which most impress us are Spiller's Diseases of the Motor Tracts, Buzzard's Diffuse and Focal Diseases of the Spinal Cord, Cushing's Tumors of the Brain and Meninges and Thomas on Diseases of the Cerebral Blood Vessels. This last is undoubtedly the most interesting chapter in the volume and contains a mass of statistical and clinical information very carefully arranged in addition to the excellent pathological section and a charming historical introduction. Nowhere else so far as we know can the student find such a thorough, authoritative and at the same time readable presentation of apoplexy. The remaining chapters are contributed by Colin K. Russel, Edwin Bromwell, Joseph Collins, Bernard Sachs, and others which want of space forbids us to discuss in detail.

As a whole the volume is well gotten up, has good illustrations, and will prove not the least valuable part of the System. The editors and publishers are to be congratulated on the work which puts the American medical profession under great obligations.

A Handbook of Medical Diagnosis for the use of Practitioners and Students. By J. C. Wilson, M. D., etc. Illustrated. Third Edition. Thoroughly Revised. $6.00 (*Philadelphia and London: J. B. Lippincott Company, 1911.*)

The popularity of this work is evidenced by its third appearance within two years. Its first appearance was noted in our pages (March, 1910). Since then the work has grown and become, it now seems to us, too cumbersome. The additions are important but it is a pity that some paring was not done. As before, the book is richly illustrated, and no doubt it will continue to find favor with the profession for it is a useful work to have at hand for reference.

A Manual of Fevers. By Claude Buchanan Ker, M. D., F. R. C. P., etc. $2.50. (*London: Henry Frowde and Hodder & Stoughton. Oxford University Press, 1911.*)

This is an excellent manual and it is a pleasure to call attention to it. After an introductory chapter, and one on The Examination of Rashes and Throats, the author successively describes measles, rubella, scarlet fever, smallpox, vaccinia, chickenpox, typhus fever, enteric fever, diphtheria, erysipelas, whooping-cough, mumps, and cerebro-spinal meningitis. The student who makes himself master of this manual will find his road to practice much smoothed. The clinical presentation of these fevers by Dr. Ker is done with brevity but skill and clearness, and his descriptions are admirable. He is already well known for his first-class text-book on Infectious Diseases, and this small manual will add to his well established repute as a physician and author.

A Text-book of Meat Hygiene. With Special Consideration of Ante-Mortem and Post-Mortem Inspection of Food-Producing Animals. By Richard Edelmann, Ph. D., Medical Counsellor; Royal State Veterinarian of Saxony; Professor at the Royal Veterinary High School in Dresden. Authorized Translation Revised for America, by John R. Mohler, A. M., V. M. D., Chief, Pathological Division, U. S. Bureau of Animal Industry and Adolph Eichhorn, D. V. S., Senior Bacteriologist. Pathological Division, U. S. Bureau of Animal Industry. Illustrated. $4.50 (*Philadelphia and New York: Lea & Febiger, 1911.*)

This is one of those standard text-books which every health officer engaged in the inspection of meat should read with great care. It is a most thorough work and for its size the best one for the average student. That a second edition has been called for is a proof of its excellence. Although written by a foreigner, it has been carefully adapted by its translators to serve its purpose well in this country.

Pain. Its Causation and Diagnostic Significance in Internal Diseases. By Dr. Rudolph Schmidt. Translated and Edited from the Second Enlarged and Revised Edition by Karl M. Vogel, M. D., and Hans Zinsser, M. D. Second Edition. $3.00. (*Philadelphia and London: J. B. Lippincott Company, 1911.*)

This work is probably not as well known as it should be to American physicians, so that we are glad to draw their attention to this new edition of a book which they will be well repaid for by mastering its many details. The author has carefully analyzed the causes of pain in the different organs and portions of the body, and in this way has made their diagnosis and significance more apparent and easily comprehended.

The Diseases of Infancy and Childhood for the Use of Students and Practitioners of Medicine. By L. Emmett Holt, M. D., etc. Assisted by John Howland, M. D., etc. Sixth Edition. Fully Revised. Illustrated. $6.00. (*New York and London: D. Appleton & Co., 1911.*)

The preeminence of this text-book has long been well recognized by the profession. There is no other treatise on these diseases by any American author which is so thorough and masterly. Doctors devoted to the study and practice of children's diseases will be especially glad to see this fresh edition, which contains much that the last edition did not have—new work that has appeared and proved of value within the last few years. Dr. Holt is to be congratulated on having secured the help of Dr. Howland, and it is a pleasure to see his name on the title page.

Manual of Pathology, Including Bacteriology, the Technic of Post-mortems, and Methods of Pathologic Research. By W. M. Late Coplin, M. D., etc. Fifth Edition. Rewritten and Enlarged. Illustrated. Price $4.50. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

For the average student in pathology this is one of the most serviceable English text-books on the subject, and as it has passed through five editions in the last fifteen years the author has kept it abreast with the times, incorporating the most important new developments. The book is divided in three parts: (1) General Pathology; (2) Special Pathology; and (3) Post-mortem and General Laboratory Technic. Almost four hundred pages are devoted to Part I, and six hundred to Part II. Attention is merely drawn to this point to indicate the relative proportion of the two subjects. Many of the illustrations are not as good as they ought to be, but the general appearance of the volume is pleasing.

The Medical History of the State of Indiana. By G. W. H. Kemper. $2.50. (*Chicago, Ill.: American Medical Association Press, 1911.*)

Some four years searching among the scanty records of all that concerns the history of medicine in America—scantiest often in details concerning the men most worthy of note—makes me keenly appreciative of the labors of any confrère in the same field and abie as well to appreciate the amount of work Dr. Kemper has put into his Medical History of the State of Indiana. He has not only gathered a valuable mass of biographical matter, but has put on record a great deal of the precious history of each county, setting forth the civic progress, climatic conditions, epidemics, the activities of medical societies, and the growth of the natural sciences, etc., thus rendering the book widely useful to future historians of the state.

In a paper on the early history of Eastern Indiana (p. 34), Dr. Joel Pennington has the following: "About New Year's I purchased from an old friend (Quaker) a hindquarter of beef, which cost, in the payment of a dollar bill, 2½ cents per pound. Pork was worth from $1.25 to $1.50 per one hundred pounds; corn, 10 cents per bushel; potatoes, 12½ cents; turnips, the same; sweet potatoes, 25 cents; wheat, 37½ cents, and all other products of the soil in proportional prices."

I suppose that great, original surgeon, Dr. John S. Bobbs, (1809-1870) is one of the most interesting characters of the state (p. 71). In 1867 he operated successfully for gall stones, entitling his paper describing the procedure in the State Transactions in 1868, a "Case of Lithotomy of the Gall Bladder." Bobbs fully appreciated the importance of medical journalism, and at his death he gave $2000 for a dispensary and $5000 for a free medical library.

That other great surgeon, Joseph Eastman, appears before us in his familiar heavy fur overcoat with its broad sealskin collar, in a satisfactory appreciative biography. The work fulfils well the function of a volume of this class in giving abundant details, and in not slighting many of the humble members of the profession. It is a work of this kind that is most appreciated by the more general historian. I have been delighted in the course of the building up of my own Cyclopedia of Medical Biographies, which is now almost through the press, to find several just such able coadjutors working in various parts of the country. Dr. Leartus Connor, lately deceased, has fully written up the history of Michigan; Dr. Slaughter has in preparation a history of medicine in Virginia.

The surgeon and the internist among medical men are content to build upon the foundations of their immediate predecessors, and to see a wide present field of utility for their services. The medical historian, however, delves in the remote past, and seeks to interest the present generation but trusts for a full appreciation of his labors to the generation yet to come which he shall never see face to face. Of all the laborers in the philanthropic field of our craft, he is the most purely altruistic, as he embalms his subjects, or rather makes them live again for future generations, as he ever cries, "Honor to whom honor is due."

Howard A. Kelly.

Haut-krankheiten Sexuellen Ursprungs Bei Frauen. Von Dr. Oskar Scheuer. Mk. 9.50. (*Berlin und Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

Dr. Scheuer has written a valuable dermatological treatise on the disturbances which are associated with puberty, chlorosis, menstruation, diseases of the sexual organs, castration, pregnancy, childbirth, the puerperium and climacteric in women. He has collected his data from a wide number of sources, and his study is an important one for all general practitioners as well as for skin specialists. The definite dependence of many of these affections on some sexual cause is not in every case well established, but this compendium of their occurrence in different periods of woman's life should prove most helpful to students in the further elucidation of the unknown origin of many of these diseases.

SEPARATE MONOGRAPHS REPRINTED FROM THE JOHNS HOPKINS HOSPITAL REPORTS.

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Pathology of Toxalbumin Intoxications. By Simon Flexner, M. D. 1 volume of 150 pages with 4 full-page lithographs. Price, in paper, $2.00.

Pneumothorax. A Historical, Clinical, and Experimental Study. By Charles P. Emerson, M. D. Price, in paper, $4.00.

Operations of 459 Cases of Hernia, in the Johns Hopkins Hospital, from June, 1889, to January, 1899. By Jos. C. Bloodgood, M. D. Price, in paper, $3.00.

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BOOKS RECEIVED.

The Goulstonian Lectures on the Sensibility of the Alimentary Canal. Delivered at the Royal College of Physicians on March 14, 16 and 21, 1911. By Arthur F. Hertz, M. A., M. D. (Oxon.), F. R. C. P. 1911. 8vo. 83 pages. Henry Frowde, London; Hodder & Stoughton, London.

Ticks. A Monograph of the Ixodoidea. By George H. F. Nuttall, M. A., M. D., Ph. D., Sc. D., F. R. S., Cecil Warburton, M. A., F. Z. S., W. F. Cooper, B. A., F. Z. S., F. L. S., and L. E. Robinson, A. R. C. Sc. (Lond.). Part II. By George H. F. Nuttall and Cecil Warburton. Bibliography of the Ixodoidea. By George H. F. Nuttall, L. E. Robinson and W. F. Cooper. 1911. 4to. University Press, Cambridge.

Scientific Memoirs. New Series. By Officers of the Medical and Sanitary Departments of the Government of India. Superintendent Government Printing, Calcutta, India.

No. 43. The Relation of Tetanus to the Hypodermic or Intramuscular Injection of Quinine. By Lieutenant-Colonel Sir D. Semple, Kt., M. D. 1911. 4°. 61 pages.

No. 44. The Preparation of a Safe and Efficient Antirabic Vaccine. By Lieutenant-Colonel Sir D. Semple, Kt., M. D., D. P. H., R. A. M. C. (Retired). 1911. 4°. 32 pages.

No. 45. Epidemic Dropsy in Calcutta. Being the First Report of an Enquiry Carried Out by Major E. D. W. Greig, M. D., D. Sc., I. M. S. 1911. 4°. 47 pages.

No. 46. Malaria in the Punjab. By Major S. R. Christophers, M. B., I. M. S. 1911. 4to. 197 pages.

No. 47. Dysentery and Liver Abscess in Bombay. By Major E. D. W. Greig, M. D., D. Sc., I. M. S., and Captain R. T. Wells, M. A., M. B., I. M. S. 1911. 4to. 78 pages.

Handbuch der biochemischen Arbeitsmethoden. Herausgegeben von Prof. Dr. Emil Abderhalden. Fünfter Band. Erster Teil. Mit 168 teils mehrfarbigen Textabbildungen. 1911. 8°. 672 pages. Urban & Schwarzenberg, Berlin und Wien.

Compendium of Regional Diagnosis in Affections of the Brain and Spinal Cord. A Concise Introduction to the Principles of Clinical Localization in Diseases and Injuries of the Central Nervous System. By Robert Bing. Translated by F. S. Arnold, B. A., M. B., B. Ch. (Oxon.). Revised by David I. Wolfstein. With seventy illustrations. [1909.] 8vo. 215 pages. Rebman Company, New York.

The Mechanism of Life. By Dr. Stéphane Leduc. Translated by W. Deane Butcher. [1911.] 8vo. 172 pages. Rebman Company, New York.

Principles of Anatomy. The Abdomen Proper, Described and Illustrated by Text and Plates. By William Cuthbert Morton, M. A., M. D. (Edin.). 1911. 8vo. 174 pages. Rebman Company, New York.

Refraction and Visual Acuity. By Kenneth Scott, M. D., C. M., F. R. C. S. Edin. With sixteen illustrations and a colored plate. [1911.] 12°. 191 pages. Rebman Company, New York.

Cesare Lombroso. A Modern Man of Science. By Hans Kurella, M. D. Translated from the German by M. Eden Paul, M. D. [1910.] 12°. Rebman Company.

The Practice of Medicine. By Frederick Taylor, M. D., F. R. C. P. Ninth edition. 1911. 8vo. 1121 pages. Macmillan Company, New York.

A Practical Handbook of the Diseases of the Ear. By William Milligan, M. D., and Wyatt Wingrave, M. D. With 239 illustrations and 6 colored plates. 1911. 8vo. 596 pages. Macmillan and Company, London.

A Pocket Medical Dictionary. Giving the Pronunciation and Definition of the Principal Words used in Medicine and the Collateral Sciences. By George M. Gould, A. M., M. D. Sixth edition, revised and enlarged, 34,000 words. 1911. 16°. 1005 pages. Blakiston's Son & Co., Philadelphia.

International Clinics. A Quarterly of Illustrated Clinical Lectures and Especially Prepared Original Articles. Edited by Henry W. Cattell, A. M., M. D. Volume III. Twenty-first Series. 1911. 8vo. 304 pages. J. B. Lippincott Company, Philadelphia and London.

Vaccine-Therapy. By William G. Dwinell, M. D. Fiske Fund Prize Dissertation. No. LIV. 1911. 8vo. Providence.

The Problem of Race Betterment. By J. Ewing Mears, M. D., LL. D. 1910. 8vo. 45 pages. Wm. J. Dornan, Philadelphia.

Surgical Applied Anatomy. By Sir Frederick Treves, Bart. G. C. V. O., C. B., LL.D., F. R. C. S. Sixth edition, revised by Arthur Keith, M. D., LL. D. Aber., F. R. C. S. Eng. Illustrated with 137 figures, including 58 in color. 1911. 16°. 676 pages. Lea & Febiger, Philadelphia & New York.

Manual of Pathology. Including Bacteriology, the Technic of Post-mortems, and Methods of Pathologic Research. By W. M. Late Coplin, M. D. Fifth edition, rewritten and enlarged. With six hundred and twelve illustrations and twelve plates, eleven of which are in colors. 1911. 8vo. 1139 pages. P. Blakiston's Son & Co., Philadelphia.

Transactions of the Philadelphia Academy of Surgery. Volume XIII. 1911. 8vo. 228 pages. Printed for the Academy, Philadelphia.

Handbook of Suggestive Therapeutics, Applied Hypnotism, Psychic Science. A Manual of Practical Psychotherapy, Designed Especially for the General Practitioner of Medicine and Surgery. By Henry S. Munro, M. D. Third edition, revised and enlarged. 1911. 8vo. 409 pages. C. V. Mosby Company, St. Louis.

A Manual of Surgery. By Francis T. Stewart, M. D. Second edition. With 553 illustrations. 1911. 8vo. 682 pages. P. Blakiston's Son & Co., Philadelphia.

Laboratory Studies in Tropical Medicine. By C. W. Daniels, M. B. Camb., M. R. C. P. Lond., and H. B. Newham, M. R. C. S. Eng., L. R. C. P. Lond., D. P. H. Camb., D. T. M. and H. Camb. Third edition, thoroughly revised, with many new and additional illustrations. 1911. 8vo. 535 pages. P. Blakiston's Son & Co., Philadelphia.

Isthmian Canal Commission. A Report on Hemoglobinuric Fever in the Canal Zone. A Study of Its Etiology and Treatment. By W. E. Deeks, M. A., M. D., and W. M. James, M. D. Published by the Department of Sanitation. 1911. 4°. 177 pages. Isthmian Canal Commission Press, Mount Hope, Canal Zone.

A Cross-Section Anatomy. By Albert C. Eycleshymer, B. S., Ph. D., M. D., and Daniel M. Schoemaker, B. S., M. D. Average Position of Organs from Eleven Reconstructions. By Peter Potter, A. M., M. D. Sections of the Female Pelvis. By Carroll Smith A. B., M. D. Drawings. By Tom Jones. 1911. Fol. 373 pages. D. Appleton and Company, New York and London.

A Manual of Pathology and Morbid Anatomy. By T. Henry Green, M. D., F. R. C. P. Eleventh edition. Revised and enlarged by W. Cecil Bosanquet, M. A., M. D. Oxon., F. R. C. P. Lond. With three hundred and fifty illustrations. 1911. 8vo. 642 pages. Lea & Febiger, Philadelphia and New York.

Immune Sera. A Concise Exposition of the Main Facts and Theories of Infection and Immunity. By Charles Frederick Bolduan. Fourth edition, rewritten and enlarged. 1911. 12°. 226 pages. John Wiley & Sons, New York; Chapman & Hall, Limited, London.

A Manual of Practical Hygiene. By Charles Harrington, M. D. Fourth edition, revised and enlarged by Mark Wyman Richardson. Illustrated with twelve plates in colors and monochrome, and one hundred and twenty-four engravings. 1911. 8vo. 850 pages. Lea & Febiger, Philadelphia and New York.

A Manual of Clinical Diagnosis by Means of Laboratory Methods. By Charles E. Simon, B. A., M. D. Seventh edition, enlarged and thoroughly revised. Illustrated with 168 engravings and 25 plates. 1911. 8vo. 778 pages. Lea & Febiger, Philadelphia and New York.

An International System of Ophthalmic Practice. Edited by Walter L. Pyle, A. M., M. D. *Pathology and Bacteriology.* By E. Treacher Collins, F. R. C. S., and M. Stephen Mayou, F. R. C. S. With three colored plates and two hundred and thirty-seven figures in the text. 1911. 8vo. 558 pages. P. Blakiston's Son & Co., Philadelphia.

A Manual of Materia Medica. By E. Quin Thornton, M. D. 1911. 8vo. 525 pages. Lea & Febiger, Philadelphia and New York.

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Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by Leighton F. Appleman, M. D. Volume III. September, 1911. 8vo. 328 pages. Lea & Febiger, Philadelphia and New York.

Manual of the Diseases of the Eye. By Charles H. May, M. D. Seventh edition, revised. With 362 original illustrations, including 22 plates, with 62 colored figures. 1911. 12°. 407 pages. William Wood and Company, New York.

Treatment of Neurasthenia by Teaching of Brain Control. By Dr. Roger Vittoz. Translated by H. B. Brooke. 1911. 12°. 117 pages. Longmans, Green and Co., London, New York, Bombay and Calcutta.

Mental Mechanisms. By William A. White, M. D. 1911. 8vo. 151 pages. Nervous and Mental Disease Monograph Series. No. 8. The Journal of Nervous and Mental Disease Publishing Company, New York.

Joint Tuberculosis. By Leonard W. Ely, M. D. Illustrated. 1911. 8vo. 243 pages. William Wood and Company, New York.

Lateral Curvature of the Spine and Flat-Foot, and Their Treatment by Exercises. By J. S. Kellett Smith, F. R. C. S. (Eng.). 1911. 8vo. 137 pages. John Wright and Sons, Ltd., Bristol; Simpkin, Marshall, Hamilton, Kent & Co., Ltd., London.

The Human Atmosphere, or the Aura Made Visible by the Aid of Chemical Screens. By Walter J. Kilner, B. A., M. B. Cantab., M. R. C. P., etc. Illustrated. [1911.] 12 mo. 329 pages. Rebman Company, New York.

An Introduction to Therapeutic Inoculation. By D. W. Carmalt Jones, M. A., M. D. (Oxon.), M. R. C. P. (Lond.). 1911. 12mo. 171 pages. Macmillan and Company, London.

Three Contributions to the Sexual Theory. By Prof. Sigmund Freud, LL. D. Authorized translation by A. A. Brill, Ph. D., M. D. With Introduction by James J. Putnam, M. D. 1910. 8vo. 91 pages. Nervous and Mental Disease Monograph Series. No. 7. The Journal of Nervous and Mental Disease Publishing Company, New York.

University of Pennsylvania. Contributions from the William Pepper Laboratory of Clinical Medicine. (Reprints.) No. 7 1909-1910. Philadelphia.

Reports from the Laboratory of the Royal College of Physicians. Edinburgh. Edited by Sir John Batty Tuke, M. D., and James Ritchie, M. D. Vols. X and XI, 1911. 8vo. Oliver and Boyd, Edinburgh.

A Manual of the Diseases of Infants and Children. By John Ruhräh, M. D. Illustrated. Third edition, thoroughly revised. 1911. 12mo. 534 pages. W. B. Saunders Company, Philadelphia and London.

Hospital Management. A Handbook for Hospital Trustees, Superintendents, Training-School Principals, Physicians, and All Who are Actively Engaged in Promoting Hospital Work. Edited by Charlotte A. Aikens. Illustrated. 1911. 8vo. 488 pages. W. B. Saunders Company, Philadelphia and London.

The Care of the Baby. A Manual for Mothers and Nurses. Containing Practical Directions for the Management of Infancy and Childhood in Health and in Disease. By J. P. Crozer Griffith, M. D. Fifth edition, thoroughly revised. 1911. 8vo. 455 pages. W. B. Saunders Company, Philadelphia and London.

Studies in Cardiac Pathology. By George William Norris. With 85 original illustrations. 1911. 4to. 233 pages. W. B. Saunders Company, Philadelphia and London.

What to Eat and Why. By G. Carroll Smith, M. D. 1911. 8vo. 310 pages. W. B. Saunders Company, Philadelphia and London.

Diseases of the Ear, Nose, and Throat. For the Family Physician and the Undergraduate Medical Student. By Henry Ottridge Reik, M. D., assisted by A. J. Neilson Reik, M. D. With eighty-one illustrations in the text and two colored inserts. 1911. 8vo. 374 pages. D. Appleton and Company, New York and London.

Practical Cystoscopy and the Diagnosis of Surgical Diseases of the Kidneys and Urinary Bladder. By Paul M. Pilcher, A. M., M. D. With 233 illustrations, 29 of them being in colors. 1911. 8vo. 398 pages. W. B. Saunders Company, Philadelphia and London.

Spirochaetes. A Review of Recent Work with Some Original Observations. By W. Cecil Bosanquet, M. A., M. D. Illustrated. 1911. 8vo. 152 pages. W. B. Saunders Company, Philadelphia and London.

A Text-Book of Medical Diagnosis. By James M. Anders, M. D., Ph. D., LL. D., and L. Napoleon Boston, A. M., M. D. With 418 illustrations in the text and 25 plates, 17 of them in colors. 1911. 8vo. 1195 pages. W. B. Saunders Company, Philadelphia and London.

Lehrbuch der Augenheilkunde. In der Form klinischer Besprechungen. Von Dr. Paul Römer. Mit 186 Textillustrationen und 13 farbigen Tafeln. 1910. 4°. 1028 pages. Urban & Schwarzenberg, Berlin und Wien; Rebman Company, New York.

Hautkrankheiten sexuellen Ursprungs bei Frauen. Von Dr. Oskar Scheuer. 1911. 8vo. 203 pages. Urban & Schwarzenberg, Berlin und Wien; Rebman Company, New York.

Kursus der normalen Histologie. Ein Leitfaden für den practischen Unterricht in der Histologie und mikroskopischen Anatomie. Von Rudolf Krause. Mit 30 Figuren im Text und 208 mehrfarbigen Abbildungen auf 98 Tafeln nach Originalzeichnungen des Verfassers. 1911. 8vo. 441 pages. Urban & Schwarzenberg, Berlin und Wien; Rebman Company, New York.

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LECTURES ON THE HERTER FOUNDATION.*

By Professor Albrecht Kossel,
Physiological Institute, University of Heidelberg, Germany.

The Proteins.

The history of physiology shows that chemistry has rendered very varied services to the former science during the different periods of its development. If we consider the history of physiology and chemistry during the Eighteenth and Nineteenth centuries, we see that organic chemistry has been gradually evolved from the study of substances of physiological importance. The simplest of the many substances produced by living organisms were isolated and systematized. From the study of these compounds a knowledge was obtained of the chemistry of carbon and of its manifold combinations with hydrogen, oxygen, nitrogen and other elements, such as could not have been derived from a study of inanimate nature. The theories of structural chemistry based upon the investigations of these substances have in turn resulted in the development of synthetic chemistry. For some time structural chemistry was busily engaged with the completion of this system and every effort was directed towards the rapid development of chemical technique. During this period pure chemistry was less intimately in touch with physiological problems. Both sciences, physiology and chemistry, seemed to drift further apart. The former devoted itself more especially to synthetic work, while the latter concerned itself principally with mechanical and physical questions and conceptions. The conviction that a comprehensive understanding of the substances taking part in vital processes was one of the most important tasks of structural chemistry was never quite extinct, but for a time no active steps were taken for its acquisition.

A new period began with the investigations upon the constitution of uric acid and other purine derivatives, upon the behavior of aromatic substances in the animal organism, and with the development of the chemistry of the carbohydrates. Theoretical chemistry began to exercise a new and powerful influence upon physiological conceptions. The growth of this influence has been due in part to the interest which theoretical chemistry has taken in determining the physical laws governing ferment action, but more especially because of the investigations upon proteins undertaken by certain prominent organic chemists.

The investigation of the chemical nature of the protein substances has made considerable strides in the two last decades and has had a corresponding influence upon physiological questions. I now propose to give a short account of the state of our knowledge in this field of work.

The development of the chemistry of the proteins has been very irregular; at times no progress appeared to be made at all and then suddenly renewed activity would result from fresh inspiration. The older investigators had already succeeded in separating certain definite chemical individuals from the mixture of substances resulting from the hydrolysis of proteins and the number of these isolated compounds increased as time went on. It was inferred that the molecular structure of the proteins was very complicated since the products of hydrolysis were so numerous and varied. The problem as to

* Delivered in the Medical Department of Johns Hopkins University, October, 1911.

how these simpler derivatives were arranged in the original protein molecule appeared to be very difficult of solution, and prior to the 90's but few investigators seriously concerned themselves with this question.

Paul Schutzenberger was the only investigator who attacked the problem with any breadth of view. His experiments, which were made during the 70's, were essentially similar in aim with those of more recent times, but his deductions were not sufficiently convincing to arouse general scientific interest nor to stimulate further work along these difficult lines of investigation.

Gradually it came to be recognized that essentially there were three separate fundamental problems which awaited solution. First, that of the composition and constitution of the fragments or products of hydrolysis; second, that of the relative proportions of these substances; and finally, that of the mode of combination and arrangement of these fragments in the protein molecule.

Knowledge of the individual fragments of the proteins is most important, since in animal metabolism we are dealing with them as reacting units. Our aim is to determine their structure and their physiological relationships. The determination of their structure is often as important as the solution of physiological questions. For chemical structure based on spatial relationships gives information about the mutual relations of the individual atomic groups, many of which are combined in the larger molecules. It indicates how a particular substance will react under given conditions and what chemical transformations it may undergo. A clear understanding of the structure of the constituents of living organisms and of their food-materials is the first step towards a knowledge of biochemical processes.

Investigation of the fragments obtained by the decomposition of protein substances has shown that the protein molecule is made up of a collection of units which in German are called *Bausteine,* or building-stones. These *Bausteine* are represented by the decomposition products which are obtained by hydrolyzing proteins by means of acids, alkalies, or by the action of enzymes. The *Bausteine* which are found in a single protein are of various kinds, but they nearly all have something in common. Most of them are characterized as α-amino-acids.

TABLE I.

CH_2NH_2 | COOH	CH_3 | $CHNH_2$ | COOH	CH_2OH | $CHNH_2$ | COOH	CH_2SH | $CHNH_2$ | COOH
Glycocoll	Alanine	Serine	Cysteine
$CH_2C_6H_5$ | $CHNH_2$ | COOH	$CH_2C_6H_4OH$ | $CHNH_2$ | COOH	$CH_2C_8H_6N$ | $CHNH_2$ | COOH	$CH_2C_3H_3N_2$ | $CHNH_2$ | COOH
Phenylalanine	Tyrosine	Tryptophane	Histidine

Glycocoll may be considered as derived from acetic acid by the substitution of one hydrogen atom by the group NH_2; alanine may be regarded as derived from glycocoll by the substitution of one hydrogen atom by the CH_3 group, while the further substitution of a hydrogen atom in alanine by the phenyl group gives us phenylalanine. If instead of the phenyl group we substitute the heterocyclic indol radical, we obtain indolalanine or tryptophane, while if we choose as substitutent a hydroxy-phenyl group, an oxygen atom, or a sulphur atom, we obtain respectively tyrosine, serine and cysteine.

If we consider these compounds as derived from glycocoll by the substitution of different organic groups, we see that the character of the molecule may be modified in two ways: First, by the introduction of acid groups we may obtain substances with pronounced acid characteristics, such as aspartic and glutamic acids; secondly, by the introduction of basic groups we obtain substances with strongly basic properties, such as we observe in the substances histidine, ornithine and lysine.

TABLE II.

COOH | CH_2 | $CHNH_2$ | COOH	COOH | CH_2 | CH_2 | $CHNH_2$ | COOH
Aspartic acid	Glutanic acid
CH_2NH_2 | CH_2 | CH_2 | $CHNH_2$ | COOH	CH_2NH_2 | CH_2 | CH_2 | CH_2 | $CHNH_2$ | COOH
Ornithine	Lysine

TABLE III.

NH_2
/
C=NH
\
NH
|
CH_2
|
CH_2
|
CH_2
|
$CHNH_2$
|
COOH
Arginine

In addition to these amino-acids we find in the protein molecule a radical of quite different character, containing one carbon and two nitrogen atoms. It is always found in combination with ornithine (diaminovaleric acid). The compound produced by the union of the amidine group with ornithine is known as arginine.

Proline, a substance with a peculiar cyclic structure, together with oxy-proline, forms a separate group. Both of these substances are derivatives of pyrrolidine.

TABLE IV.

CH_2 — CH_2
| |
CH_2 CH — COOH
\ /
NH
Proline

It is very probable that atomic groups are present in the protein molecule which have up to the present evaded detection. It is unlikely, however, that these substances are of much quantitative importance. It is true that the structure of one product of protein hydrolysis, diaminotrioxydodecoic acid, with the empyrical formula $C_{12}H_{26}N_2O_5$ has still to be elucidated.

The complexes which are formed by the union of these various atomic groups or *Bausteine* are known as the albumins or proteins. These proteins may contain either few or many of these constituent groups. Thus we know proteins which yield not more than five of these groups while others yield all of them. Where the succession of carbon atoms is interrupted by the presence of other atoms it is usually found that the molecule will undergo disruption at this point, either within the living organism or without.

We find that there are some proteins which fail to yield certain cleavage products, while in some other cases we encounter cleavage products which are so exceptional that we are not justified in considering them as typical protein derivatives. Glucosamine, an amino derivative of glucose, is a case in point.

The quantitative relations of the cleavage products derived from any particular protein are believed to be constant. The following table indicates clearly that different proteins yield widely different amounts of the various cleavage products. It is possible to estimate these cleavage products with accuracy only in the case of a few of them. In most cases the figures in the table represent the yield of substance capable of separation rather than the amount actually present, which naturally must be somewhat greater. However, the results are amply sufficient to indicate the wide differences in composition of different proteins.

TABLE V.

The Figures Indicate the Yield of the Cleavage Product in Gm. from 100 Gm. of the Protein.

	Casein (Osborne and Guest).	Wheat gliadin (Osborne and Guest).	Silk fibroin (E. Fischer and A. Skita).	Histone (Kossel, Kutscher, Abderhalden, Rona).	Sturine (Kossel, Weiss, Dakin).	Salmine (Kossel and Dakin).
Glycocoll	0	0	36	0.5	....	0
Alanine	1.50	2.00	21	3.46	pres.	0
Valine	7.20	3.34	....	....	0	4.3
Leucine	9.35	6.62	1.5	11.8	pres.	0
Proline	6.70	13.22	(0.3)	1.46	0	11.0
Phenylalanine	3.20	2.35	1.5	2.2	....	0
Glutaminic acid	15.55	43.66	....	3.66	....	0
Aspartic acid	1.39	0.58	pres.	....	....	0
Cystine	?	0.45	....	....	0	0
Serine	0.50	0.13	1.6	....	0	7.8
Tyrosine	4.50	1.20	10.0	6.31	0	0
Oxyproline	0.23	....	....	....	....	....
Histidine	2.50	0.61	....	1.21	10.3	0
Arginine	3.81	3.16	1.0	14.36	57.9	87.4
Lysine	5.95	0	....	7.7	7.9	0
Tryptophane	1.50	[1.00]	....	....	0	0
Diaminotrioxydodecoic acid	0.75	....	....	....	....	....
Ammonia	1.61	5.22	....	1.66	0	0

These results force us to the conclusion that the chemical structure of proteins with varying properties possess entirely different structures. We must also conclude that the atomic groupings of the various cleavage products actually exist as such in the protein molecule; for on hydrolysis of the same protein they are always obtained in constant quantity. It is improbable that complicated intramolecular changes accompany their formation, for they are obtained from proteins not only by chemical reactions at high temperatures, but also at body temperature by the action of enzymes.

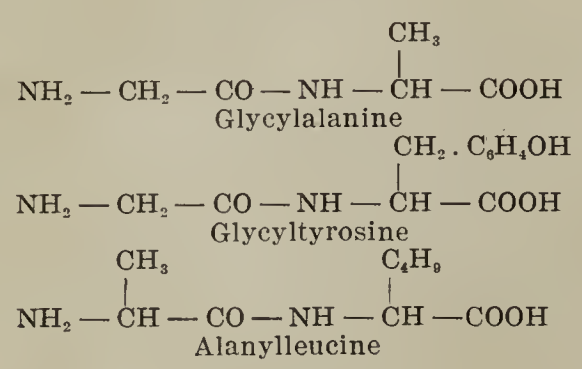
The conception of the proteins as substances formed by the union of simple cleavage products indicates a certain resemblance between them and the carbohydrates. The complex carbohydrates which are stored in the tissues, *i. e.*, the polysaccharides, are similarly derived from the union of groups containing five or six carbon atoms which are analogous to the cleavage products of the proteins. These groups are united with each other by means of oxygen atoms and may be readily separated by means of the hydrolyzing action of acids or enzymes. The large organic molecules which are built up as the result of the activities of living cells are thus seen to possess a certain similarity as regards their component parts. They are to a certain extent formed by the loose union of simple groups in such a way that they may easily undergo change and rearrangement in the course of the metabolic changes occurring in the living body.

This relationship is also recognizable in the case of the fats. The cleavage products are in part larger, for they include molecules containing 16, 18 or even more carbon atoms arranged in a straight chain. The cyclic structures present in related substances, such as chlosterine, play a less active rôle, presumably because these continuous carbon groups are less easily decomposed by the living organism.

The recognition of the fact that the proteins, like the polysaccharides, are made up of simpler derivatives, leads us to consider the question as to how these derivatives are united with one another. I first began my investigations on the protamines with the hope of obtaining a solution of the constitution of these simple protein substances, and came to the conclusion that the union of the *Bausteine* was effected by means of the imid groups. Emil Fischer, through a series of masterly investigations, has definitely shown that this type of combination is found in all protein substances.

We can distinguish two forms of this imid combination. The one is produced by the union of a carboxyl group with an amido group, with elimination of the elements of water. In this case a carbonyl group is adjacent to the imido group . . . CO—NH—C . . . The second form is produced by the union of an amino group with urea, water being eliminated in this case also. In this way a guanidine grouping is produced: NH_2—CNH—NH—C . . . Th. Curtius, and especially Emil Fischer, have shown by their synthetic experiments that it is possible to combine the cleavage products of the proteins according to the first form and to obtain substances which in their properties closely resemble the more complex protein derivatives. Furthermore Fischer and his co-workers have actually succeeded in separating from proteins derivatives which yield on hydrolysis only two to four cleavage products. It has thus been possible to make a comparison between the synthetic products and similar substances derived by the hydrolysis of proteins and so to place the constitution of the latter on a firm basis. The following formulæ give certain examples of polypeptides obtained from proteins.

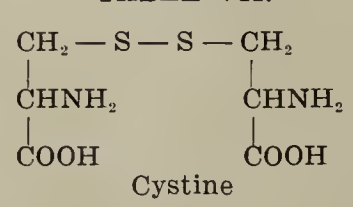
TABLE VI.



The second type of imid combination was recognized by E. Schultze and was confirmed later by synthesis. Its resolution takes place under different conditions from those affecting the first type. It is more resistent to hydrolysis by means of dilute acids and only undergoes cleavage when subjected to the action of a specific ferment.

The imid form of combination is not the only one effecting the union of carbon groups in the protein molecule. Baumann's determination of the constitution of cystine, which has since required but slight modification, was made in the 80's. He found that this cleavage product consisted of two carbon groups united by means of a sulphide linkage. The resolution of this linkage is effected by reduction and not, as in the other cases, by hydrolysis.

TABLE VII.



Let me illustrate the complexity of the constitution of the proteins by a few examples. First of all I should like to draw your attention to a group of proteins called *protamines*. In my opinion these substances are of great importance and I have been engaged upon the investigation of them for some time.

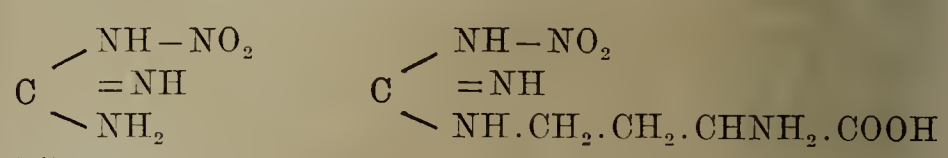
The protamines are distinguished from other proteins by two peculiarities: one is that they have a simpler constitution than any other proteins with which we are at present acquainted; the other is that they possess strongly basic characteristics. The protamines form a group possessing a very limited distribution. Up to the present they have only been found in the spermatozoa contained in the testicle of certain fish. We can distinguish various types of protamines and the group is connected with the more complex or "higher" proteins by means of substances of intermediate complexity.

The most varied protein constituents take part in the formation of the protamines: the mono-amino-acids, including alanine, serine, tryptophane, tyrosine, amino-valeric acid, amino-caproic acid and proline—the di-amino-acids, including ornithine and lysine, also histidine. In union with ornithine we find the "urea-forming" group, the whole forming arginine. All of these groups are not formed in the same protamine molecule; indeed the protamines represent combinations containing a few of these groups.

The simplest variety of protamine I may call the salmine type. This type predominates in protamines which are obtained from the testicles of mackerel, herring, pike, and salmon. Salmine, which was isolated by Miescher and called "protamine," was the first of these substances to be discovered. It belongs to the class just mentioned, together with clupeine, esocine and scombrine. In a second class of protamines we place cyclopterine from Cyclopterus Lumpus and one of the protamines obtained from the testicles of the carp, namely, β-cyprinine, and possibly also crenilabrine from Cr. Pavo. In a third class of protamines we have only one representative, namely α-cyprinine. Sturine, a protamine derived from the testicles of the sturgeon, belongs to a fourth class.

The relationships between the members of the first class are simplest. These substances on hydrolysis yield a large quantity of arginine as well as various amino-acids; alanine, amino-valeric acid, serine and proline. The quantitative relations are such that upon hydrolysis 8/9 of the total nitrogen is found in the form of arginine. Since arginine contains four atoms of nitrogen, we infer that in these protamines there is one molecule of mono-amino-acid for every two molecules of arginine. Judging by experience and by our present knowledge of the mode of union of various groups we are forced to conclude that at least two arginine groups are united together. Hence di-arginide or poly-arginide groups are present in the molecules of these protamines. Certain observations, the details of which I cannot at present enter upon, indicate that these protamine molecules are composed of di-arginyl-alanine, di-arginyl-serine, di-arginyl-proline, di-arginyl-amino-valeric acid, etc., and the results of the analysis of the hydrolytic cleavage products confirms this assumption. The union of these various *Bausteine* is effected in such a manner that the strongly basic groups are still free. Goto's experiments upon the capacity of clupeine to combine with acids showed that each arginine molecule corresponds to one alkali equivalent.

Recently with E. L. Kennaway and A. T. Cameron I have made additional observations which also show that one of the amido-groups in the arginine contained in the clupeine molecule must be free and able to react. It is for instance not difficult to introduce a nitro-group into clupeine and on hydrolysis of the nitro-clupeine, nitro-arginine is found among the cleavage products. Nitro-arginine is a substance which apparently must be regarded as a derivative of the asymmetric nitro-guanidine described by Thiele:



Nitroguanidine Nitroarginine

From these results and from experiments on the action of nitrous acid on protamines we infer that it is the amino-group in the arginine contained in the molecule of the protamines of the salmine group which is responsible for the basic properties of the whole molecule. In the protamines of other classes different groups may influence the basicity of the molecule. Thus Hirayama and Pauly have shown that the iminazol ring present in the histidine contained in sturine is free and is not

bound in peptide fashion. The same is true of the amino-groups of the lysine present in α-cyprinine—a simple protamine containing but little arginine. Also the lysine contained in sturine has one or two free amino groups.

While some of the amino-groups of the protamines are free, and are not linked with other *Bausteine,* the carboxyl groups on the other hand are mostly combined. This follows from Goto's observations on the diminishing alkalinity of clupeine upon hydrolysis. This is apparently due to the resolution of ester-like groupings, containing serine.

The application of these various observations and deductions to the protamines shows clearly that the examination of these simple proteins is capable of indicating the lines of investigation which will be helpful in determining the composition of the more complex ones. The propriety of grouping together the protamines and the more complex proteins, which in the past has sometimes been questioned, cannot now be doubted. Many facts indicate this most clearly—not the least important being the discovery of proteins intermediate in complexity between the protamines and the more complicated proteins.

In *typical* proteins the mono-amino-acid groupings are so much increased in quantity and complexity that they are of paramount importance. In certain kinds of typical proteins, however, the basic properties, dependent upon the presence of free amino-groups are very well marked. This is the case with the proteins known as *histones.* The cleavage products of the histones are very rich in basic di-amino-acids, although to a lesser extent than those of the protamines. While in the protamines almost 89 per cent of the total nitrogen appears in the form of arginine, the histones yield about 27 per cent in this form; this is however more than one finds in most typical proteins. But there are certain other proteins which contain just as much arginine without possessing the properties of the histones. The peculiarity of histones consists not so much in the presence of a certain number of basic substances among the cleavage products, but rather in the presence of *free basic* groups in the histone molecule itself. In addition the histones have a few other peculiarities in common with the protamines, such as the property of uniting with other proteins to form sparingly soluble precipitates. Their physiological relations also point to resemblances with the protamines; especially the fact that they appear in combination with nucleic acids as constituents of the cell-nucleus.

The more complicated proteins exhibit great differences among themselves, for they vary not only according to their physiological relationships, but also according to the conditions of their formation and the functions they subserve in the living organism. I have already indicated how a complex protein may lack one or another of the *Bausteine* and how in other cases one or another may predominate. I should like to draw your attention to a few examples of this kind.

A striking example was found by Kutscher and myself in our work upon the distribution of lysine. We found that this *Baustein* which is so commonly present in most proteins was entirely absent from a vegetable protein characterized by its solubility in alcohol. From the later investigations of Hopkins, Osborne and Abderhalden it was found that the tryptophane and glycocoll groupings were also absent from the same protein. The systematic examination of the cleavage products of thoroughly typical proteins such as egg-albumin, casein and serum albumin has also demonstrated the absence of glycocoll. Many proteins fail to yield cystine and tyrosine. On the other hand no substance of protein character has ever been found which did not contain the arginine grouping.

In the early stages of the development of protein chemistry it was found necessary to distinguish two kinds of proteins—"the true proteins" and "the albuminoids." This distinction was made partly upon chemical grounds and partly for physiological reasons. The true proteins were supposed to contain all the essential constituents of the protein molecule while albuminoids, on the other hand, lacked some of the typical *Bausteine.* The former were regarded as of full nutritive value while the latter were not. But some proteins were classified as albuminoids which did not lack any of the typical cleavage products, but which for some other reason, such as difficult solubility, could not take part in the metabolism of some species of animals. Keratine is an example of this kind. The so-called true proteins were, however, regarded as of equal value from a metabolic point of view. Such a classification as this can no longer be maintained and the theory of albuminoids must be abandoned. The construction of a system for the classification of constituents of the living body based upon a mixture of chemical and physiological criteria was bound inevitably to lead to confusion. If today we relegated to one group gelatine, elastine, the proteins of silk and perhaps the protamines as well, we should obtain a class of proteins which could only be characterized by the fact that the individual members had nothing in common with each other.

The complexity of structure possessed by the proteins is much increased by the fact that the molecules which already are very large, readily combine with each other or with other substances. This is readily seen, for example, when protamines combine with the proteins—a precipitate being formed at once on mixing feebly alkaline solutions of the two components. The combination of histones with other proteins may be observed in the same way. It is not unlikely that similar compounds are formed when, in the course of chemical analysis, animal tissues are brought in contact with aqueous solutions. It is probable, moreover, that conditions exist in the animal organism which permit of the formation of these compounds. Hoppe-Seyler suggested the name "proteide" for these complex substances consisting of a protein in combination with an additional substance called later a "prosthetic" group.

In the class of proteides we must include the blood colouring matters, mucoids, nucleins and many other tissue constituents. Our knowledge of these substances is but slightly developed, but we are already aware of their great complexity due to the variety of added prosthetic groups.

The simplest members of this group are those in which iodine, iron or some other element is combined with the protein molecule. Protein complexes containing iodine are found in invertebrate marine animals and also in the thyroid gland.

In the first of these cases Wheeler, Jamieson and Mendel have shown that the iodine is combined with the tyrosine complex, for on hydrolysis the iodine containing protein yields di-iodo-tyrosine.

In hæmoglobin we find complex organic groups united with the proteins. These groups are themselves colored and the color of hæmoglobin itself is due to them. Chemical investigations have shown that the prosthetic group of hæmoglobin is a complex containing 34 carbon atoms containing several pyrrol rings and also iron in organic combination.

The nucleins, which are characteristic constituents of cell nuclei, contain as the prosthetic group the so-called nucleic acid, which is also very rich in heterocyclic rings. In addition it contains other remarkable groups. I found as constituents of nucleic acids a number of organic substances which are now grouped together under the name of purine derivatives, including adenine, guanine and their derivatives, hypoxanthine and xanthine. I also found the pyrimidine derivatives thymine and cytosine and in addition an atomic complex which must be regarded as belonging to the carbohydrate group. This complex group of molecules is also combined with phosphoric acid, the elements of water being eliminated. Nuclein is formed by the union of this complex nucleic acid with protein. The proteide nuclein may be obtained artificially by bringing together solutions of the two components when nuclein immediately separates out as a precipitate.

A prosthetic group closely resembling nucleic acid is found in guanylic acid derived from the pancreatic gland. The composition of guanylic acid is similar to but simpler than the nucleic acid previously mentioned. Besides these we know of the existence of yet another series of phosphorus containing proteides, but the nature of their prosthetic group is still quite unknown.

Reactions entirely similar to those of the nucleic acids may also be observed in the case of chondroitic acid which is found most abundantly in tissues such as cartilage. Like nucleic acid, chondroitic acid combines directly in aqueous solution with proteins to form a proteide insoluble in water. Some of these artificially prepared proteides are readily resolved into their components, as is the case with salt-like combinations. The protamine present in the substances formed by its union with more complex proteines may readily be recovered on subjecting the compound to peptic digestion. Under these conditions the more complex proteide undergoes hydrolysis while the protamine resists the action of the pepsin and may be separated by the use of suitable precipitants. On the other hand there are other proteides in which the prosthetic group is so firmly bound to the protein that vigorous chemical methods must be employed to effect their separation. Under these conditions one obtains a complex mixture of cleavage products, from both prosthetic group and protein, the separation of which presents great practical difficulties.

On this account it has proved impossible to separate with certainty the intact prosthetic group from many mucoids and phospho-proteins.

F. von Muller and Lanetti have shown that a glucosamine group is present in many mucines and mucoids and, indeed, the distribution of this carbohydrate group has proved to be so wide that many authors are inclined to include it among the typical protein cleavage products.

These chemical investigations which I have briefly put before you today raise the question as to whether the different protein substances which we have been able to separate from animal or vegetable tissues, owing to their varying chemical characteristics are really to be regarded strictly as chemical individuals. Are our criteria which we employ for judging of the purity of these substances in their preparation and purification sufficiently stringent?

We must admit that the larger and more complicated the molecule the more readily certain differences in composition escape one's attention. Thus, the large atomic complex made up of many similar groups, such as we find in the proteins, might undergo substitution of one group for a similar one with so little effect upon the properties of the protein that they might evade detection. We must also admit a certain variation in the constitution of proteins analogous to the small variations which we observe in different organized structures. It is probable, therefore, that the proteins which we may separate from animal organs are not always chemical individuals in the strict sense of the word. Many small analytical variations may be ascribed to this cause.

These considerations do not, however, seriously detract from the value of investigations in the field of protein chemistry. If we consider our analyses as applying to representatives of certain types of proteins rather than to chemical individuals in all cases there can be little doubt that we shall be able to profitably speculate as to the general laws governing the building up of proteins from their simple cleavage products.

The results which have already been obtained have been sufficient to stimulate the study of metabolic problems and to present many new points of view. I shall hope to show you this in my next lecture.

II.

We must infer from the constant occurrence of the proteins that the phenomena of living matter are dependent upon the presence of these substances. But we know very little of the significance of the proteins in connection with the manifestations of life. It is clear that their rôle is a complex one. They fulfill a part of their function while, in the form of complete molecules, they take part in the vital processes. Another part of their functions concerns their ability to act as receivers of substances for synthetic purposes, for the taking up from time to time of substances of low molecular weight, the more readily transportable atomic groups, and the storing of the energy contained in them.

The functions of the proteins are in part dependent upon their physical characteristics, in part upon their chemical properties. In many cases we encounter them taking part in the formation of tissues of definite form and shape, in the same way as cellulose is formed among plants and chitin among the invertebrates. We see how their physical properties are made

use of in the resistance of keratin, the elasticity of elastin, the transparency of the refractive part of the eye.

We all know how easily the proteins react with mild chemical reagents, how readily they are altered by acids and alkalies and the ease with which they yield compounds, metallic oxides, acids and other substances. Some of these derivatives are often encountered in the tissues and secretions. The fact that proteins are so prone to undergo chemical change is to be referred to the presence of carboxyl, amido and imido groups, the occurrence of these groups in many proteins being definitely proved. I have already mentioned that in some proteins the basic properties predominate, in others, the acid; the former is the case with the protamines and histones while casein and similar proteins belong to the latter group. These properties must also assert themselves in the living cell, although we must admit that we know nothing of how this takes place. We must assume that the chemical changes that are concerned in the formation of new organic parts, with the production of "immune substances" or similar bodies and with the acceptance and transmission of stimuli, cannot take place independently of the proteins, but we are at present unable to formulate any picture of the chemical mechanism of these processes.

One might imagine that a comparison of the chemical structures of the proteins with their occurrence in the organism would shed light upon these and similar problems. The results of such researches, however, are but few, since the methods of investigation are primitive. Notwithstanding this, I believe that one may draw some very noteworthy conclusions from series of observations upon young cells especially rich in nuclei. In the growing animal we invariably observe a storing up of nitrogen. This nitrogen in the proteins is partly in the form of arginine, partly also as lysine and histidine, and in addition we find a large quantity of nitrogen-rich substances in the prosthetic groups of the nuclein substances. This is especially characteristic of those portions of the body substance which are concerned with reproduction and growth.

On the other hand we observe that when protein substances have been elaborated for purely mechanical functions they are commonly deficient in basic constituents. This is the case with elastin and with silk-fibroin, for in these protein molecules the monamino acid groupings predominate to such an extent that the nitrogen-rich groupings seem to be almost absent. These results clearly indicate how investigations upon the structure of the proteins can yield results having a direct bearing upon the problems concerning plasma and cells. The development of protein chemistry has, however, proved of greater value in the study of metabolic processes than in any of the other branches of physiology.

In my last lecture I have drawn attention to a property shared by the proteins with the other substances of high molecular weight present in the organism. This consists in the numerous atomic complexes linked together by means of oxygen atoms or NH groups, and I have already indicated that these complexes are readily set free during metabolic changes and subsequently reunited. These changes also take place in the process of transportation of these large molecules. The proteolytic ferments are the agents used by the organism for the breaking down of the proteins into their *Bausteine*. They attack the proteins in much the same way as *oxylytic* ferments attack complex carbohydrates. In the latter case disruption occurs at the point where hexose or pentose groups are linked by means of an oxygen atom, while in the case of the proteins scission takes place at the point where the various groups are united by NH linkages. The action of the different *iminolytic* ferments may be more or less far-reaching. Thus the disintegration of the protein molecule may yield complex products of high molecular weight, such as the albumoses and peptones—this is known to be the case in peptic digestion. Other ferments are unable to attack the unaltered proteins, but are able to act upon their decomposition products. From investigations made upon the behavior of polypeptides it has been found that their constitution and configuration determine whether they are attacked by proteolytic ferments or not. The behavior of arginine, a substance derived from the union of ornithine with a urea-forming group, is especially noteworthy. It is unattacked by hydrolysis with acids and with most active ferments, but is readily decomposed by a specific ferment, arginase, which is found in certain organs of animals and plants.

The activation of these ferments takes place either inside or outside the living cell at definite times according to the needs of the organism. What are the conditions which determine these needs of the organism? Is the breaking down of the larger molecules simply for the purpose of facilitating their transport? Or is the breaking down of the proteins by means of enzymes into their components merely the first step toward their complete decomposition?

The point of view necessary for the proper consideration of these problems has only been obtainable since the newer development of protein chemistry. So long as we were unaware of the great difference existing between individual proteins it was impossible to understand why protein food should be decomposed before being converted into body protein. The demonstration of such a far-reaching decomposition of proteins in the intestinal tract of higher animals follows from several observations, of which I shall refer to one only. Szumowski made the following experiment in my laboratory: He fed geese with corn (maize), until they had materially increased in weight, *i. e.* they had stored up nutrient material. He then killed the animals and examined the organs for the presence of the peculiar protein of corn—the so-called zein. This examination was the more easy since zein is completely different from the animal proteins. Its ready solubility in alcohol serves for its separation from the proteins present in animal organs, and, in addition, zein is characterized by the absence of the lysine group. When the administration of zein was by way of the alimentary canal, *i. e.* the natural method, this protein was never detected in the organs of the geese. When, on the other hand, the zein was introduced into the circulation directly, it was possible to demonstrate its accumulation in the liver. This experiment leads us to the conclusion that in the herbivorous animal a rearrangement of the food proteins must take place so that from the lysine-free zein we

obtain the differently constituted animal protein. Similar transformations must take place in plant seedlings when the protein constituents of the young plant are formed from the proteins of the endosperm, or similarly in the case of the chick in its development at the expense of its albumin reserves. In the latter case all the different proteins found in the blood, nervous system, connective tissue, and muscle are formed from the proteins of the yolk and white of egg. In the same way the keratin of the feathers, the gelatin yielding substances, or the globin of the red-blood cells, must be formed from the same mixture of food proteins. The composition of these various proteins is so different that their formation must be preceded by a breaking down of the chemical structure of the food protein before reconstruction with new protein is possible. Similar rearrangements must take place in every growing organism and are especially prominent in those cases in which one organ is developed at the expense of another whether under normal or pathological conditions. From investigations by Wakeman we must conclude that in phosphorus poisoning the tissues become poorer in arginine, hence it is probable that proteins poor in arginine are formed. The opposite change is seen in the formation of the male sexual products. The Rhine salmon is particularly well adapted for demonstrating this change. This fish takes no nourishment during the time of the ripening of the testicles, and takes the protein material for the formation of sperms from its own body, especially from the muscles. In this way from the arginine-poor proteins of the muscles is obtained the arginine-rich and completely differently constituted protein making up the head of the sperm. This protein belongs to the class of protamines. The diminution in muscle substance has been quantitatively determined by Miescher and in my laboratory Weiss has carried the investigation a step further by determining the distribution of arginine during the process. It was found that the amount of arginine originally present in the muscle before wasting is sufficient to cover the arginine requirements of the growing testicles. It is therefore unnecessary to assume that this protein constituent is specially synthesized during the ripening of the testicle. It appears more probable that the constituents derived from the decomposition of the muscle protein are utilized for the formation of the new protein. The greater part of the mono-amino acids of the muscle protein do not appear in the protamine molecules; apparently they are utilized during the period of testicle formation for the nourishment of the rest of the body while the nitrogen-rich part is used for the formation of the new protein. These changes which accompany the ripening process differ somewhat among the various families of fishes. In all cases basic groups predominate in the newly formed molecules. A larger or smaller amount of arginine is invariably present, but the atomic groups other than arginine vary widely, as I have already mentioned in my first lecture. These rearrangements presuppose a prior decomposition, but we have no knowledge as to how far the original molecule undergoes disintegration. It is possible that the molecule is completely resolved or it may be that decomposition takes place to only a limited extent. The same problem presents itself in the consideration of the formation of other proteins, as we shall see in a moment.

In the foregoing discussion we have been considering the proteolytic changes in the animal organism and we have seen that the decomposition of protein molecules in the animal body may take place by the action of hydrolytic ferments, the elements of water being taken up. From what has gone before, it is also clear that the living organism has the power to bring about the reverse process, namely the reunion of these products by hydrolysis with elimination of water.

Physiological chemists have long known that the amino group of glycocoll is capable of union with a carboxyl group through biochemical action. The formation of hippuric acid by the union of the amino group of glycocoll with the carboxyl group of benzoic acid is an example of this. In the same way the organism of the bird effects the union of another protein derivative, namely ornithine with benzoic acid. These changes are analogous to the formation of proteins from their cleavage products. Notwithstanding this, however, the conception of a synthesis of protein in the animal body was not entertained by those of the older physiologists interested in the problems of metabolism. It was generally held that the proteins partly unchanged and partly in the form of albumoses and peptones, were absorbed from the products of digestion, and that the portion of the proteins which underwent hydrolysis by means of the digestive ferments could no longer serve for synthetic purposes. It was observed that albumoses and peptones disappeared when brought in contact with intestinal mucous membrane. This was assumed to be due to their being taken up by the intestine in the same way as in normal absorption. The albumoses and peptones were assumed to be bound by union with the histological elements of the mucous membrane. The observations of Kutscher and of Cohnheim necessitated a modification of these views. Kutscher showed that the decomposition processes occurring in the intestines were much more far reaching than had been previously supposed, while Cohnheim showed that the disappearance of peptone when brought in contact with intestinal mucous membrane was not due to its absorption, but rather to its decomposition. A ferment called erepsin is present in the mucous membrane which is able to effect the complete decomposition of peptone into its *Bausteine*. These *Bausteine* rapidly disappear on absorption since they cannot be detected in the blood.

A series of experiments to determine the question of the regeneration of protein in the living body were begun about this time. The cleavage products of proteins were fed to animals and observations upon the nitrogen balance were then made. Is it possible to bring about an increase in body protein as the result of the feeding of these protein *Bausteine?* If this could be demonstrated, the power of the animal body to effect protein synthesis would be proven.

The first experiments of this kind were successfully carried out by O. Loewi. He fed a dog with the products of autolysis of pancreatic tissue containing all the protein cleavage products, with a resulting increase in body protein. These experiments have been frequently repeated and modified and there

is now no question of the formation of new protein in the animal body from completely hydrolyzed protein cleavage products *i. e.* from its *Bausteine.* The experimental method required considerable development and especial efforts were made to obtain a preparation which on the one hand contained all the *Bausteine* of protein, and on the other hand was *completely* hydrolyzed. Convincing proof of the correctness of Loewi's conclusions was given by Abderhalden and his co-workers. Meat subjected to the action of various proteolytic ferments was used as starting material. It was soon found that the disappearance of the biuret reaction was no certain indication of complete hydrolysis, polypeptides being formed which do not give the biuret reaction. Sörensen's method of formaldehyde titration was used successfully for determining the point of complete hydrolysis. It was found to be immaterial whether the protein was hydrolyzed by ferments or with acids, provided that those atomic groups which were destroyed by the boiling with acids were replaced. The experiments were carried out on men, dogs, rats and mice, and not only was the nitrogen-balance maintained, but nitrogen was actually stored in the body. These results can hardly be interpreted otherwise than through the assumption of a synthesis of protein from the *Bausteine* which had been fed.

From these results follows the consideration of the second question as to how far the proteins undergo cleavage in the course of normal digestion. At present we are unable to answer this question with certainty. From the results of Borchardt we must assume that under certain circumstances even large protein complexes which still give the biuret reaction are capable of passage through the intestinal wall. Borchardt fed a cat with elastin, or hemi-elastin—its first decomposition product—and some hours after feeding was able to detect this latter albumose-like substance in the blood and organs of the animal. The detection of the hemi-elastin was rendered possible owing to the excellent precipitation reactions of this substance. Since we must regard elastin as a normal food constituent, the possibility of the absorption of these substances of high molecular weight must be admitted. But the possibility of the utilization of these substances for purposes of protein synthesis is by no means disproved. It is probable that the breaking down of these atomic groups may take place not only in the lumen of the gut or in the intestinal wall, but also in other organs. It is certain, however, that the conditions for a very far reaching decomposition of protein are most favorable in the intestine.

In the light of these results and with special regard to the ease with which proteins undergo both decomposition and synthesis in the animal and vegetable organisms we are led to consider the question of the importance of the proteins in metabolism rather from the point of view of their *Bausteine* than from the proteins themselves. Within what limits is it possible for one cleavage product to replace another? And are these cleavage products of unequal value from a metabolic point of view?

If these cleavage products were mutually interchangeable without restriction we should be obliged to infer that the proteins themselves were mutually interchangeable in metabolism. As a matter of fact we have long known that this is not the case. It is well known that gelatine cannot completely replace other food proteins, and it was natural to correlate this observation with the absence in the composition of gelatine of the two *Bausteine,* tyrosine and tryptophane. If this assumption were correct we should expect other proteins lacking in certain *Bausteine* to be incapable of serving as an exclusive source of protein food. My investigations with Kutscher have shown that the alcohol soluble proteins of cereals, for example zein, are free from lysine, and Hopkins and Wilcocks showed the absence of tryptophane as well. As a matter of fact Hopkins and Wilcocks and Henriques concluded from their experiments that zein was unable to replace completely other proteins in the food supply of mice and rats. Abderhalden and Glamser obtained similar results when they attempted to feed a dog with a mixture of substances derived by the complete hydrolysis of silk fibroin. The nitrogen balance was negative—that is to say, the cleavage products of silk fibroin were unable to serve as an exclusive source of protein nutriment.

Experiments of this character raise the question as to whether it is not possible to supply the missing cleavage products. As long ago as the seventies experiments were made in which tyrosine, tryptophane, cystine and other amino-acids were added to gelatin in order to determine their effect upon the nitrogen balance. The latest and most complete experiments of this kind were carried out by Abderhalden and Manolin. They found that in the case of the dog at least two-thirds of the protein nitrogen necessary for the maintenance of nitrogen balance could be obtained from completely hydrolyzed gelatin to which a certain quantity of other amino-acids had been added. Hopkins and Wilcocks had previously made experiments upon the feeding of mice with zein and their results indicated the importance of tryptophane in animal metabolism. Zein, as I have already mentioned, yields neither tryptophane nor lysine. They found that those mice which were fed upon zein as their sole protein food developed a peculiar condition of torpor which was not observed in the control animals. "For several days before death the mice were exceedingly inactive and made no movement when touched or handled. When in this condition the ears, feet and tail were cold to the touch, the eyes half closed and the coat glairy." The mice in all cases succumbed when fed upon zein without addition of tryptophane. On addition of tryptophane, however, they lived for a longer period. "The addition of tyrosine which is already present in zein has no such effect." That these phenomena were really due to lack of tryptophane was shown by the subsequent experiments of Henriques. He demonstrated the inability of zein to serve as a sole source of food protein. But, if, instead of zein, he fed another vegetable protein closely resembling zein in composition and, like the latter, yielding no lysine, he found that not only did the rats live but, when they consumed a sufficient quantity of the gliadin, nitrogen was actually stored. The most important difference in the composition of the two proteins is that gliadin contains the tryptophane group while zein does not. The importance of tryptophane is emphasized by the latest

experiments of Abderhalden. He fed dogs a mixture of the cleavage products of casein and brought the animals into nitrogen equilibrium. On feeding an equal quantity of cleavage products of casein from which the tryptophane had been removed, the nitrogen balance became negative, but on replacing the tryptophane nitrogen equilibrium was once more attained.

Hopkins and Wilcocks have suggested some very interesting views upon the rôle of tryptophane in animal metabolism. They consider that the fragments of the protein molecule may subserve other uses in the organism than "in the repair of tissues and in supplying energy. . . . . It is highly probable that the organism uses them in part for more immediate needs. . . . . Even when tissue equilibrium is not maintained, the presence or absence of some one amino-acid in the diet may affect most materially the survival period and general well-being of an animal." Accordingly the authors advanced the hypothesis that tryptophane "serves as a basis for the elaboration of a substance absolutely necessary for life—something, for instance, of an importance equal to that of adrenalin." They suggest that "the tryptophane is directly utilized as the normal precursor of some specific hormone or other substance essential to the processes of life." If the food materials do not contain the precursors of such hormones, the organism suffers injury, just as is the case when the organs forming the hormones cease to functionate.

While these experiments have shown that tryptophane is essential to the maintenance of life, Henriques' experiments with gliadin indicate that lysine may be dispensed with. One is inclined to assume that those protein *Bausteine* which possess a similar chemical constitution play a similar rôle in metabolic processes. The amino-acids of the aliphatic series may possess similar physiological significance. If we assume this, the fact that lysine may be replaced by homologous cleavage products becomes intelligible, whilst tryptophane stands in a class by itself both chemically and physiologically.

One may now consider the question of the possible conversion of one protein cleavage product into another, and also the possibility of the synthesis of these cleavage products themselves in the animal body. As a matter of fact investigations carried out during the last ten years have clearly demonstrated that the synthetic functions of the animal organism are not restricted to the assembling of ready formed protein fragments. As in the case of the vegetable organism, the formation of long carbon chains or of complicated heterocyclic systems from simple carbon compounds may take place in the body of higher animals. The prosthetic groups of the proteides are formed in this way. As an example of this I will refer to some experiments carried out in my laboratory a long time ago. Alexander Tichomiroff investigated the eggs of the silk-worm before and after the development of the young worms and found that purine derivatives, which are scarcely detectable in the undeveloped eggs, are present in large amounts in the bodies of the young animals. I obtained similar results in the case of hens' eggs.

A still more complicated prosthetic group is found in the red coloring matter of the blood. On decomposing this substance one can obtain dimethyl-ethyl-pyrrol and recent investigations have shown that four of these pyrrol rings united in a system containing thirty-four carbon atoms form the colored component of hæmoglobin. The formation of this complicated substance is effected not only in the body of the chick as soon as the area vasculosa is formed, but also takes place actively in the body of higher animals when, after severe loss of blood, it is necessary to replace the lost hæmoglobin. It is impossible to assume that the pyrrol derivatives necessary for this purpose exist preformed in the body.

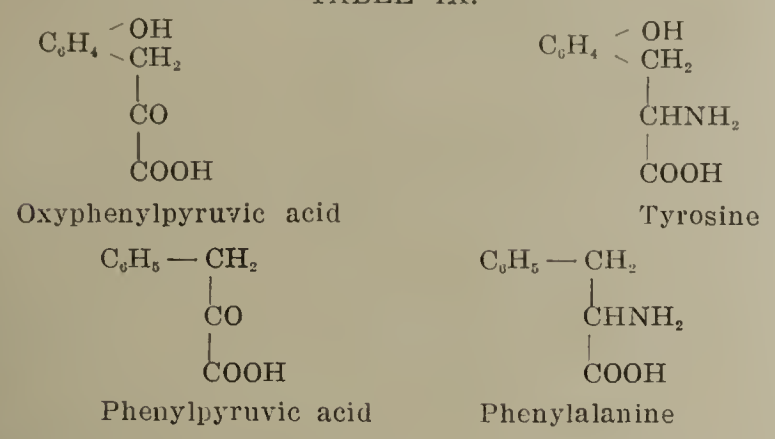
One may imagine that the synthetic activities of the body are regulated exactly according to the demands made upon it and that the power of ready synthesis is not made use of when the substance is contained in the food.

These questions gain in importance when we consider investigations which have been recently made upon the capacity of the animal body to form amino-acids. Experiments by Wiechowski and by Magnus Levy had already shown that the body could furnish more glycocoll than corresponded to the amount it had received. It would be possible to explain this in other ways than by synthesis, as, for example, by the breakdown of higher amino-acids. Knoop, however, has recently shown that nitrogen may be united with carbon with formation of an amino-acid in the course of animal metabolism. This reaction was observed on the administration of a ketonic or oxy-acid. Knoop made his experiments with γ-phenyl-α-ketobutyric acid and γ-phenyl-α-oxybutyric acid. From both of these substances the acetyl derivatives of phenyl-α-amidobutyric acid was formed and excreted in the urine. These experiments were extended by Embden and Schmitz. They perfused surviving livers with blood containing ketonic acids. In this way they demonstrated the formation of tyrosine from p-oxyphenylpyruvic acid, and phenyl-alanine from phenylpyruvic acid. Alanine was formed in good quantity from pyruvic acid and, as in the case of tyrosine and phenylalanine, was obtained in the naturally occurring optically active modification. Knoop concluded from his experiments that lactic acid which, as is well known, may be formed during muscular activity, and which has such a wide distribution in the body, might by a similar reaction be converted into alanine. Embden and Fellner were able to demonstrate this change by means of perfusion experiments. The following structural formulæ will render these reactions more intelligible.

TABLE VIII.

CH_3 | $CHOH$ | $COOH$ Lactic acid	CH_3 | CO | $COOH$ Pyruvic acid	CH_3 | $CHNH_2$ | $COOH$ Alanine
$C_6H_5CH_2$ | CH_2 | $CHOH$ | $COOH$ Phenyl-α-oxybutyric acid	$C_6H_5CH_2$ | CH_2 | CO | $COOH$ Phenyl-α-ketobutyric acid	$C_6H_5CH_2$ | CH_2 | $CHNH_2$ | $COOH$ Phenyl-α-amidobutyric acid

TABLE IX.



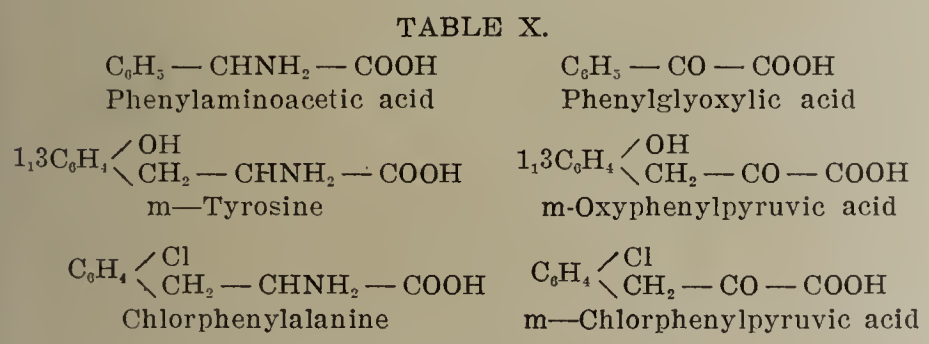
Embden was able to show that on perfusing a liver for an hour and a half a part of the glycogen was converted into alanine through the intermediate formation of lactic acid.

These results suggest that certain parts of the protein molecule originate from the carbohydrates. A similar relationship is indicated by the interesting observations of Knoop and Windaus upon the action of ammonia upon glucose, resulting in the formation of the iminazol ring—methylglyoxal being apparently an intermediate step in the reaction. The iminazol ring is characteristic not only for histidine but is also contained in the purine derivatives.

Investigations upon the fate of various constituents of the protein molecule undergoing decomposition in the animal organism have similarly revealed new and important relations existing between various tissue constituents. The detection of the intermediate steps in these rearrangements is of course only possible under special conditions. These conditions are found in cases in which the decomposition processes are incomplete because of disturbances of metabolism, like alcaptonuria and cystinuria. The same is true of experimental conditions permitting a separation of a part of the metabolic processes such as the perfusion of isolated organs, or of the study of chemical substances containing a nucleus or side-chain resistent to the disintegrating forces of the animal organism. This is the case with cyclic derivatives such as tyrosine, phenylalanine and tryptophane, either formed in the animal body or artificially introduced.

These substances first of all lose their amino group, which in the case of the protein derivatives are always found in the α-position. According to Neubauer and Flatow the amino group is replaced by oxygen so that a ketonic acid is formed from the amino-acid. This was observed in the case of phenylaminoacetic acid which was converted primarily into phenylglyoxylic acid when administered to rabbits. In the same way the feeding of m-tyrosine was followed by the excretion of a ketonic acid, m-oxyphenylpyruvic acid, while chlorphenylalanine gave chlorphenylpyruvic acid.

TABLE X.



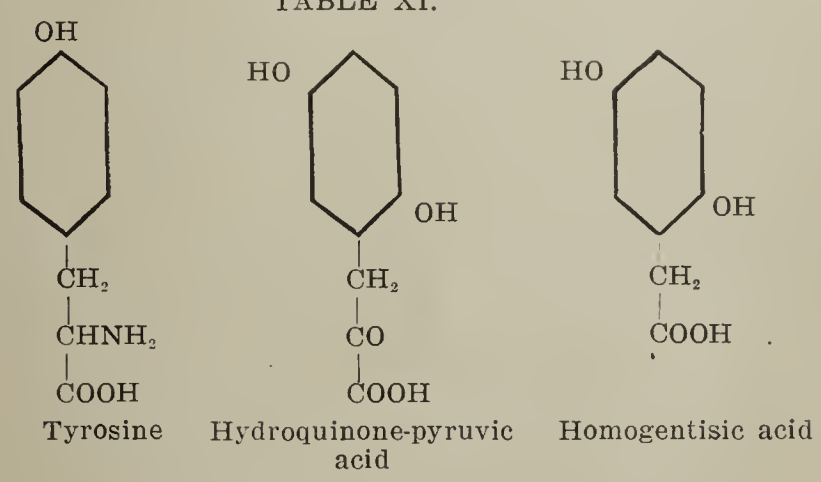
The process by which these substances are formed is the exact opposite of the previously mentioned synthesis of amino-acids in the animal body.

The further decomposition of the ketonic acids takes place with the removal of carbon dioxide and conversion of the CO into a COOH group.

Thus for example Neubauer showed that phenylpyruvic acid, derived from phenylalanine gives acetoacetic acid, when perfused through a surviving liver. The benzene ring is completely destroyed. The experiments of Dakin and Wakeman make it appear probable that of the four carbon atoms in acetoacetic acid two are derived from the benzene ring and two from the side-chain.

I may refer to the production of homogentisic acid. This acid is formed from tyrosine probably with intermediate production of hydroquinone-pyruvic acid, the three carbon side-chain being oxidized to an acetic acid group. At the same time another process takes place in the benzene ring—the hydroxyl group present in the p-position disappearing and two new OH groups appearing in positions 2 and 5.

TABLE XI.



A number of experiments have been made upon alcaptonurics in order to test these conceptions. Benzene derivatives of various kinds have been fed to persons showing this abnormality of metabolism in order to determine which of them are convertible into homogentisic acid. It was found that only those substances containing an amido or hydroxyl group or an oxygen atom attached to the centre carbon atom of the three carbon side-chain (*i. e.* in the α-position) were precursors of homogentisic acid.

Through the reactions previously mentioned an acid is formed containing one carbon atom less than its precursor which may then undergo further oxydation. In the case of normal carbon chains of the aliphatic series further oxydation takes place in the β-position. Carbon compounds with long chains of this kind occur in proteins to a limited extent only, as in lysine and in the ornithine contained in arginine. Knoop has drawn attention to the fact that arginine may yield guanidinebutyric acid which on oxidation would yield guanidineacetic acid. The latter substance, according to Jaffe, may be converted into creatin in the animal body by taking up the methyl group.

Investigations of this kind have demonstrated the formation of tissue products from fragments of the protein molecule.

This is also true of Friedmann's observations upon the formation of taurine from cystine.

When we consider the results obtained from the co-operation of chemistry and physiology, we notice certain marked changes in our ideas. Chemistry has shown that the proteins are made up of a certain number of units or *Bausteine* and that the differences in these *Bausteine* and the variations in their mode of linkage is responsible for the great variety of proteins. The resolution of a protein into simpler molecules or *Bausteine,* a process which is readily accomplished in the animal organism by means of ferments, involves the evolution of but little heat. Physiology has shown that the animal organism has not only the means of resolving the larger molecules into smaller ones, but also can bring about the reverse process. Furthermore it appears that the protein *Bausteine* play a rôle in animal metabolism not only as parts of the protein molecule but also as independent units. Feeding experiments have shown that glycocoll, ornithine and cystine may combine with certain substances administered to animals. In normal as well as diseased animals and especially in sprouting plants free amino acids of all kinds are to be found as well as more complicated molecules such as arginine, alanylhistidine and asparagine. There is no reason why the appearance of these substances should be considered solely from the standpoint of protein synthesis or decomposition. Hitherto the appearance of protein *Bausteine* in the living organism has always been ascribed to protein decomposition. But this supposition is unjustified. We must rather assume that these *Bausteine* may appear and disappear in the body without at any time forming part of a protein molecule. And further we may suppose that only under certain circumstances, for definite physiological purposes, are these independent groups stored in a collected form—the protein substances. This point of view does not exclude the possibility of the proteins as a whole taking part in important biological processes; but in general the problems concerning the proteins may be resolved into a series of simpler questions more accessible to research.

Thus the protein *Bausteine* are also the *Bausteine* of living material—of protoplasm. They are analogous to the other constituents of protoplasm which, like them, are capable when necessary of combining to form larger units—for example the phosphatides, the nucleins, fats and polysaccharides. All of these larger units are readily decomposed and as easily reformed by the tools of living substances—the ferments.

When we wish to consider the physiological rôle of protein substances, we must carefully distinguish between those cases in which the proteins act simply as the sum of their constituent *Bausteine* and those in which the special nature and mode of combination of these *Bausteine* are of greater importance. The use of protein as food is an example of the first case. The structural peculiarities responsible for the individuality of a given protein are destroyed by digestion and none of its characteristics remain except so far as they appear in the quantitative relation of its *Bausteine.* These *Bausteine* are absorbed and for the nutrition of the organism it is obviously a matter of indifference whether they arose from this or that combination. They are in all cases utilized according to the requirements of the organism.

If a protein reaches the body fluids without undergoing this process of dissolution, the conditions are altogether different. The protein may then exert special action depending on its structure. I would like to illustrate this by an example.

When arginine, valine or another *Baustein* found in the protamines is injected in rather large doses into the circulation the blood pressure is not particularly affected nor is any poisonous action observed. But W. H. Thompson has shown that if we inject into a dog 0.7 gram of a protamine formed by the union of these *Bausteine* there is a very considerable fall of blood pressure and paralysis of the respiration ending in the death of the animal. If we convert the protamine into protone by partial hydrolysis, the change involving a resolution of some but not all of the molecular combinations, it is found that the substance is physiologically almost inactive. The original protamine possessed the property of forming insoluble precipitates with other proteines in feebly alkaline solutions. The loss of this chemical property on dissolution of the protamine molecule is coincident with the loss of physiological activity.

This example shows us that by the union of various *Bausteine* groups may be formed conferring special chemical properties upon the whole molecule which can be recognized by their physiological actions. In the particular example cited the action was poisonous and harmful, but in other cases the effect produced by intact protein molecules may be a beneficial one. In all of these cases the action of the protein is not that represented by the sum of its *Bausteine,* but its properties are determined by its own structure. At present we cannot fully comprehend the rôle of the proteins, but we must assume that many of the enigmatical properties of living matter depend on this activity of *intact* protein molecules. We can obtain some idea of the possible variety in the combinations of the protein *Bausteine* by recalling the fact that they are as numerous as the letters in the alphabet which are capable of expressing an infinite number of thoughts. Every peculiarity of species and every occurrence affecting the individual may be indicated by special combinations of protein *Bausteine,* that is to say by specific proteins. Consequently we may readily understand how peculiarity of species may find expression in the chemical nature of the proteins constituting living matter, and how they may be transmitted through the material contained in the generative cells. Moreover it may be possible to obtain an explanation of the specific reactions of blood plasma based on the peculiarities of definite proteins; and by so doing we shall bring another group of phenomena nearer to chemical comprehension.

But it is not my intention on this occasion to follow the attractions of hypothesis at greater length. It must suffice to express the conviction that within the scope of protein chemistry we shall find new paths leading through the entire domain of biological research.

In conclusion, I wish to fulfill a pleasant duty in again expressing my thanks to my friend, Dr. H. D. Dakin, who has translated these lectures.

THE PATHOLOGY OF FAT METABOLISM.

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The accumulation of fatty substances in diseased cells is one of the most frequent of morbid changes. It is likewise one of the most generally misunderstood. It is a very widely held conception of the pathological processes which lead to the gross appearance of fat in cells that such fat is the direct product of protoplasmic degeneration. This conception, false though we now believe it to be, was taught by the text-books for more than fifty years, with the result that the term "fatty degeneration" has become, in the hands of the general medical writer, a careless designation for a variety of cell injuries associated with the appearance of fat. There are many terms in medicine which, like life preservers, are useful in an emergency. They have no precise, well-defined meaning and are often employed to enable a writer to make with ease a difficult landing. "Fatty degeneration" is such a term.

Fatty changes are in reality the most delicate indication of cell injury, with consequent impaired metabolism that we possess, but their correct interpretation demands a knowledge of the normal and abnormal metabolism of the fats.

The investigations of recent years have added richly to our knowledge of the pathology of fat metabolism, a result largely due to the application to the subject of chemical and physico-chemical methods. It is to some of the newer conceptions to which these advances have led that we shall devote our attention in this paper.

The Chemical Nature of the Fatty Substances Found in the Body.

Until within recent years writers, in discussing the pathology of fat metabolism, have dealt with substances of simple chemical constitution, namely, the fatty acids, neutral fats and soaps. But we have gradually learned the great importance to the economy of another large and heterogeneous class of substances, the so-called "lipoids" or fat-like bodies, whose chemistry is by no means so simple or well understood. Exact chemical knowledge of the structures and properties of many of the substances classed as "lipoids" is still lacking; enough, however, is known to permit the bio-chemist to form a provisional classification. I shall follow, in so far as it seems of aid to the pathologist, the classification of fatty substances proposed recently by Rosenbloom and Gies.[1]

Ivar Bang[2] has defined "lipoids" as those compounds which are soluble in organic solvents, as ether, alcohol, chloroform, benzine, etc. It will be observed that this definition of lipoids embraces also the fats as usually understood. This immediately leads to confusion. Rosenbloom and Geis suggest the term "lipins" (analogous to proteins) as a substitute for "lipoids," and attempt a chemical classification of all fatty substances, similar to the present official classification of the proteins. Some of the terms which they use are new, but they are descriptive and do not differ confusingly from other designations now in use. The general adoption of these terms is not to be expected, may indeed be undesirable, but they furnish a logical working classification and as such have been employed in this paper. Their classification follows:

LIPINS (LIPOIDS).

I. Natural Aliphatic Lipins.

A. *Simple Lipins.*—All of these contain *carbon, hydrogen* and *oxygen,* but are free from *phosphorus, sulphur,* and *nitrogen.*

(a) Fatty acids, such as butyric and palmitic; various unsaturated acids as oleic and linoleic; and hydroxy acids of all these types.

(b) Salts and esters of the acids just spoken of in the preceding group.

(1) Soaps, as sodium oleate.

(2) Waxes.

(3) Fats and fatty oils. These neutral fats, or triglycerides, are esters of the trihydroxy alcohol, glycerol. Representatives of the class commonly found in the body are tri-butyrin, tri-palmitin and tri-olein.

B. *Conjugate Lipins.*—Natural compounds of simple lipins with non-lipin substances or radicles. All of these compounds contain *carbon, hydrogen* and *oxygen,* and practically all of them contain *nitrogen.* These substances, with those in Group II, A, constitute the group of so-called "lipoids"—a term without a definite chemical basis. (*Protargon* is a *mixture* of several conjugate lipins.)

(a) *Proteolipins.*—Compound lipins *containing protein radicles* (lecitho-proteins), such as lecithalbumins and ovo-vitellins. (These products may be only mechanical mixtures of proteins and lipins.)

(b) *Glycolipins.*—Compound lipins that are free from protein radicles but which *contain carbohydrate radicles,* such as the "cerebro-galactosids" represented by phrenosin. The substances in this group are *free from phosphorus* (Thudichum's "Cerebrosids").

(c) *Phospholipins.*—Compound lipins that are free from protein and carbohydrate radicles, but which *contain phosphoric acid radicles.* Lecithin, cuorin and sphingomyelin are examples (Thudichum's "Phosphatids").

II. Natural Carbocyclic Lipins.

A. *Sterols.*—Natural terpeno-alcoholic derivatives. They contain *carbon, hydrogen* and *oxygen,* but are *free from phosphorus, sulphur, and nitrogen.* Leading members of the group are *cholesterol,* iso-cholesterol, koprosterol and sitosterol. These substances are Abderhaldens "sterins," and with the conjugate lipins (Group I, B) constitute the so-called "lipoids."

B. *Esterols.*—Esters of sterols, such as cholesteryl palmitate in lanolin and cholesteryl oleate in blood.

C. *Cholates.*—Terpeno—acid derivatives of *hepatic* origin, probably from sterols or sterol radicles.

(a) Cholic acids (and their simple biological salts), such as cholic and choleic acids.

(b) Bile acids (and their biological salts), such as glycocholic and taurocholic acids.

The only other lipins of direct interest to the pathologist are the enigmatical "lipochromes," of undetermined composition, called by Rosenbloom and Gies chromolipins.

It is not possible in a paper of this kind to discuss in detail the separate classes of lipins; it will facilitate subsequent discussions, however, if we pause at this point to compare the structural formula of a typical simple lipin with that of a well-known conjugate lipin. Let us select one of the neutral fats, triolein, found so widely distributed throughout the body, and compare its structure with that of the conjugate phospholipin, lecithin, which likewise has a wide cellular distribution.

Triolein:

$$\begin{array}{l} CH_2O.OC.C_{17}H_{33} \\ CH.O.OC.C_{17}H_{33} \\ CH_2O.OC.C_{17}H_{33} \end{array}$$

Lecithin:

$$\begin{array}{l} CH_2O.OC.C_{17}H_{33} \\ CH.O.OC.C_{15}H_{31} \\ CH_2O.—P=O \\ \qquad\qquad\quad \wedge \\ \qquad\quad OH \quad O.C_2H_4 \\ \qquad\qquad\qquad\qquad > N(CH_3)_3 \\ \qquad\qquad\qquad HO \end{array}$$

It will be noted, on comparing the two, that whereas in triolein the three hydroxyl groups of the tri-acid alcohol glycerol are replaced by three oleic acid radicles, in lecithin each of these hydroxyls is replaced by a different radicle. One of these radicles is probably always that of oleic acid, another that of some other fatty acid, while the third, which characterizes the substance, is a phosphoric acid radicle, which in turn is joined to the base cholin. In spite, however, of the more complicated structure of lecithin, it is obvious that it is very closely related to the simple neutral fats. Such a relationship reveals to us how the body may synthesize from relatively simple substances highly complex cell constituents. We are prone to think of metabolic processes as largely katabolic, whereas it is certain that anabolic synthetic processes precede the katabolic ones, often producing as end results very complex structures.

Cholesterol ($C_{27}H_{44}O,H_2O$) is another lipin which is a constant and important cell constituent. It is a mono-hydroxy terpeno-alcohol, and forms esters with fatty acids just as does the tri-hydroxy alcohol glycerol. Some of these esters exhibit very singular physical properties which we shall soon have occasion to study in more detail.

This brief chemical survey of the fatty substances will meet our present needs; those more interested in this phase of the subject will do well to consult the monographs of Bang and Leathes.[3]

We are fortunate in possessing several very reliable methods for the *morphological* study of fatty changes in cells. Just how fortunate we are will be the more appreciated when we contrast the relatively advanced condition of our knowledge of pathological fat metabolism with the almost utter ignorance which enshrouds the subject of cloudy swelling of cells. In another place[4] I have discussed the relative merits of the various methods for the morphological study of fatty substances, and since the necessary details are readily accessible in the technical manuals, these methods, important though they are, need not detain us at this time.

The Physiological Occurrence of Lipins in the Body.

There is a question, often neglected, but of the greatest importance, in a study of pathological fatty changes in cells, which is directly connected with the morphological study of of fatty cell-inclusions, and that is the physiological occurrence of fat in the various cells of the body. The lipins are one of the three great sources of the body's food supply, and they are normally present in some form in all cells. It is not generally recognized, however, that microscopic fat globules may be present physiologically in varying amounts in all gland cells. Cells of this type are not using their maximum energy all the time, hence it is quite common for a gland like the pancreas, for example, to show very considerable variations from time to time in its microscopically visible fat-content.

This phase of the question is well illustrated by the conditions present in seminiferous tubules of the normal testicle. Such a testicle, stained for fat, shows in certain tubules not actively engaged at the time in sperm-formation, many rather large fat globules situated in the Sertoli cells. These globules are usually ascribed to a "fatty degeneration" of the Sertoli cells. With the advent of spermatogenesis, these large globules break into smaller ones and gradually pass into the spermatocytes and spermatids. As this takes place, the fat alters its character from that of a neutral fat, or simple lipin, to one of the more complicated conjugate lipins, probably lecithin. The fully matured spermatozoa are peculiarly rich in fatty matter which further strengthens our belief that the fat assimilated by the Sertoli cells, or sperm-nourishing cells as they are called, is used during spermatogenesis as nutriment for the developing spermatozoa. The conditions found in cryptorchid testes furnish additional proof of what has just been said. In this condition, as is well known, all cells of the sperm-forming series have completely disappeared, thus removing the normal physiological outlet for the fat assimilated by the Sertoli cells. As a consequence, the Sertoli cells become engorged with neutral fat droplets, and chemical anaylsis shows that the percentage of fats in cryptorchid pig testes is almost double that found in the normal organ. Here again authors insist that the Sertoli cells are in a condition of "fatty degeneration," and this despite the fact that such Sertoli cells contain healthy nuclei, and nowhere present evidences of cellular disintegration.

Examples of such errors arising from a failure to appreciate the rôle of fatty substances in the body's metabolism could be

multiplied. It is not so long ago that the adrenal was regarded as showing a constant normal "fatty degeneration" of its cortex, and the corpus luteum cells were thought to be in the same desperate condition.

The fat which is assimilated by the healthy cell is quickly changed to a combined state in which it is no longer possible to render it visible by any micro-chemical means at our disposal. This combined fat forms a large item among the total constituents of the cell. The kidney normally contains from 15 to 23% (dried weight) of fat in this invisible condition. Now the fat deposited in the great fat-depots of the body (subcutaneous and subserous tissues, omentum, mesentery, peri-renal fat, etc.) is readily available for the body's nutriment, and disappears with starvation. It is *labile* fat. Fat in the invisible, combined condition of which we have spoken is on the contrary highly *stabile,* the cells clinging to it with the greatest tenacity even in extreme starvation.

The Pathological Occurrence of the Simple Lipins.

We have seen that the term "fats" in its broader modern meaning includes a great variety of substances which vary considerably from each other in their chemical constitution. Their solubilities in organic solvents, however, separate them fairly sharply from the carbohydrates and proteins, and permit of their classification in one large heterogeneous group. These fats, or lipins, are primary and essential constituents of the cell, and occur, with quantitative and qualitative variations, in all the cells of the body. They may or may not be microscopically visible.

It remains for us to consider the occurrence of the various kinds of lipins throughout the body under pathological conditions. This is at once one of the most interesting and difficult of pathological problems, and, in spite of recent great advances, it is by no means a closed chapter.

In the first number of his Archiv (1847) Virchow divided the forms of pathological fatty changes into two groups—fatty infiltration and fatty degeneration. Virchow taught, as the term fatty infiltration indicates, that fat may infiltrate a cell from without, the cell remaining healthy, and perfectly capable of returning under more favorable conditions to its normal state. This change he considered to be only a slight deviation from the physiological fat-infiltration seen in adipose tissue, or from the fatty infiltration of the intestinal mucosa and liver during digestion.

Fatty degeneration, however, he conceived to be a far more serious lesion of the cell—a true necrobiotic process. "Unter den nekrobiotischen Prozessen ist der unzweifelhaft am weitesten verbreitete und fast wichtigste im Verlaufe aller bekannten cellularen Störungen die fettige Degeneration." ("Die Cellularpathologie, etc.," 1862.)

He regarded the accumulation of fat in this condition as due to a direct degeneration of the cell protoplasm into fat. This conception has become classical, and has been, until very recently, the orthodox teaching. Whether this doctrine is absolutely erroneous or not is impossible to state with certainty. It is assuredly quite conceivable that fat may be derived from so huge a complex as the proteid molecule, and indeed some bacteria and fungi are capable of effecting this change, but there is not the slightest evidence that such a transformation ever takes place in the body. There is, on the contrary, a great deal of excellent evidence that the accumulation of fat in cells is always an infiltrative process. Some of this evidence we shall now review.

Cell injuries caused by a great variety of substances are associated with fatty accumulations. Conditions such as phosphorous and arsenic poisonings; intoxications with bacterial toxins, especially when accompanied by fever; the excessive use of alcohol; deranged function of certain glands with internal secretions; the various types of anemia—these and many other conditions may cause cellular injuries which are accompanied by visible fatty accumulations.

Confronted with the fatty liver of phosphorous poisoning, or of chronic alcoholism, or with the fatty mottled heart of pernicious anemia, what proof have we that the abnormal amounts of fat which are so obvious represent infiltrations from extra-cellular sources, and are not derived from the transformation of the cytoplasm of the injured cells into fat? This question has provoked a tremendous amount of investigation, some results of which are among the most brilliant of medical science.

Lebedeff, in 1883, was the first to oppose Virchow's conception of "fatty degeneration" with substantial scientific proofs. He fed starved dogs on linseed oil and, after phosphorous poisoning, found the fatty condition of the liver largely due to the presence of this oil. Lebedeff concluded that the fatty liver of phosphorous poisoning was due to a mobilization of the depot-fats in the liver, and other organs. It is a surprising fact, but nevertheless true, that an animal fed upon a foreign fat will store this fat largely as such in its fat-depots. This result has been repeatedly confirmed.

Some fourteen years later Rosenfeld, in a series of very careful researches, demonstrated conclusively this transportation of fat in phosphorous poisoning, and since then many confirmatory details have been added by other investigators. One of Rosenfeld's striking experiments was this. He starved dogs until their body fat could not be further reduced, and then fed them lean meat and an easily identified foreign fat, such as linseed oil (which has a low melting point and can combine with much iodine) or mutton tallow (which has a high melting point and a low iodine number). Under these conditions, the animals stored the foreign fat in their fat-depots and liver. After a few days' starvation (to remove the fat from the liver) the animals were poisoned with phosphorus, which produced a fatty condition of the liver and other viscera. An examination of this fat revealed that it was not typical dog fat, as it should have been if it were a result of proteid degeneration, but was largely composed of the foreign fat which had been previously fed. Furthermore, animals which were in a state of starvation failed to develop fatty livers when poisoned. These and other interesting results have been confirmed by Febiger in chickens and rabbits, and by Taylor, and Athanasiu, in frogs.

It seems well established, then, that in fatty cellular changes we are dealing with a process of fatty accumulation or infiltration and not a degeneration in the sense of Virchow. There is likewise much morphological evidence for this view, but we need not pause to discuss it at this time.

Upon analyzing organs showing typical fatty infiltration and comparing their total fat with the fat content of normal organs, Rosenfeld made the seemingly contradictory discovery that the total fats of a fatty infiltrated organ are not greater in quantity, and may be less, than normal. All the facts, however, are easily harmonized by a consideration of the metabolism of the normal cell.

Fat is being constantly taken up from the nutritive fluids of the body either as soluble fat, or as glycerol and fatty acids, which latter may be in the form of soaps. This fat is contained in the cell in an invisible form, probably in chemical combination, for as has been noted, a kidney which contains no visible fat under the microscope may yet contain normally from 15 to 23% (dried weight) of fat upon extraction. This is the stabile fat of which we have spoken, and it is in part so firmly bound to the proteins that peptic digestion is necessary for its complete liberation. Now the assimilation of fat, and its further utilization by the cell, are certainly two largely independent processes. Normally, they are nicely regulated so that the intake and utilization balance. But if the cell is poisoned or if through anemia its oxidative powers are decreased, this metabolic balance is disturbed. Fat continues to enter the cell through the activities of the highly resistant cell lipase, but once there, the disorganized dissimilative functions of the cell are unable to utilize it—fat accumulates. We may not in the given instance of a certain toxin be able to say just what injury it produces in the cell which disturbs the normal fat metabolism; our ignorance of the normal structure and metabolism of the cell is too profound for that. But it requires no great flight of imagination to conceive that substances so foreign to the normal content of a cell as arsenic or chloroform or bacterial toxins, may produce very great alterations in the physical and chemical constitution of the cell, with consequent disturbance of metabolism. An explanation of Rosenfeld's observation that fatty-infiltrated organs may show no increase in their total fats follows from what has been said. It is an accepted biologic principle that cell intoxicants act primarily as stimulants to increased metabolic activity. Hence we may accept that the first effect of a poison will be an increased demand for food on the part of the cell. In response to this demand, fat leaves the storehouses and is carried by the blood to the various organs. The injured cells are using more fat, and until the injury actually advances to a degree where metabolism is seriously disturbed, the increased intake of fat is speedily utilized. If the intoxication is severe, however, a time soon comes when some cells are no longer able to convert the fat taken from the blood into the invisible, combined form. It is conceivable, however, that fat which has already been elaborated by the cell is subsequently utilized, so that while we see more and more fat, it does not necessarily follow that in the end the affected organ will contain absolutely more fatty matter. If the injury ultimately results in a complete destruction of the normal molecular arrangement of the cell, some of the combined fats present in the nucleus and cytoplasm will become visible. That is apparently what happens in post mortem autolysis, a subject to which we shall soon return. The accumulation of fat in the cells of the body is, however, a vital process; dead cells may show fatty deposits, but it seems certain that such fat was assimilated during the life of the cell and not after death.

The Pathological Occurrence of More Complex Lipins.

In the foregoing discussion of fatty infiltration the term fats (or lipins) has been employed without seeking to be more specific, following the usage which prevailed until within recent years. Now, however, it is necessary to consider the pathological occurrence of not only the neutral fats, fatty acids and soaps, but of some other very important members of the group of lipins. Only a few of these are chemically well defined enough to permit at present of very exact studies. They present to both the chemist and the pathologist serious difficulties in that they are usually present as mixtures, the components of which mutually influence each other, and many are soluble in exactly the same solvents, rendering their separation difficult and often impossible.

The nomenclature of new and complex subjects is often involved, and the terminology of the lipins is no exception to the rule. Some writers speak of "fats and lipoids" in an attempt to separate the neutral fats, and their components, from the remaining lipins. Others use the term lipoid as a collective name for all fatty substances. Both usages are inexact and misleading. It seems to me that we can only hope to escape unnecessary confusion by adopting some classification embracing all fatty substances, and then refer by name to the separate members of the group. This I have tried to do by adopting what seems to be the most helpful classification available. In a subject which is so rapidly advancing, any classification must be recognized as largely tentative and provisional.

Aside from the simple lipins (neutral fats, fatty acids and soaps), only two other groups need enter into a pathological discussion of the lipins. These are the phospholipins (phosphotids), which are characterized by the presence of a phosphoric acid radicle in their molecule (one of the lecithins will serve as an example), and the compounds of the terpeno-alcohol, cholesterol.

All fatty changes in living cells are the result of infiltration, that is, the fats are of exogenous origin. The character of these fatty substances varies, however, and it is very important for us to learn to detect the different varieties of lipins which are encountered under pathological conditions in the body, for they are of varied significance. There is one characteristic of certain lipins which permits their detection at once, even when they are mixed with others. For example, if we scrape some of the fatty, necrotic material from an area of arteriosclerotic degeneration and examine it under the microscope, we shall find among the detritus masses of fatty matter and

cholesterol crystals. Upon examining the same specimen between the crossed Nicol prisms of a polarizing microscope a singularly beautiful phenomenon is observed. Standing forth from the intense blackness of the unilluminated microscopic field are many small, brilliantly glistening, globular bodies, many of which on closer examination, show a dark Maltese cross dividing the globules into four highly refractile sectors. This is the phenomenon of double refractivity or anisotropism and is a property of crystalline substances. The globules which we have just described, though, are fluid, for they constantly assume, especially on warming, a spheroidal shape and are mobile. They are indeed *fluid crystals,* as was first pointed out by Adami and Aschoff. Physical chemists are familiar with many such bodies (Lehmann: Flüssige Kristalle. Leipzig, 1904). Their solubilities in fat solvents and their staining reactions leave no doubt that these anisotropic globules belong to the group of lipins.

Kaiserling and Orgler first directed modern attention to these peculiar anisotropic lipins, and they have been carefully studied by Aschoff,[5] Adami,[6] Kawamura[7] and others. It seems fairly well established that whereas several individual lipins, and mixtures of these, may show anisotropism (as for example certain soaps, sphyngomyelin and possibly lecithin, phrenosin, cholesterol and cholesteryl esters), only certain of these substances, namely, cholesterol and its compounds, show constantly and typically the phenomenon of double refractivity at the temperature of the body. This has led Aschoff to divide fatty infiltration qualitatively into "Glycerinesterverfettung" and "Cholesterinesterverfettung." Certain other characteristics aid in the differentiation of cholesteryl esters. When they are warmed the phenomenon of anisotropism disappears, only to return on cooling in a more outspoken and beautiful fashion. Other lipins showing anisotropism do not lose this property on warming. Cholesterol compounds are less soluble than neutral fats in the ordinary fat solvents, and stain rather yellow than red with Sudan iii. They become gray rather than black when treated with osmium tetroxide. On freezing, or fixing in formalin, they may assume solid crystalline forms, which on warming pass again into the globular, fluid crystal phase. Most other fixatives destroy at once this anisotropic property, and it is not seen after staining with the usual fat-stains. It remains after staining with Nile blue sulphate. Material to be examined for anisotropic lipins may be teased in the fresh state and examined in glycerin or water, or where the maintenance of histological relations is desired, frozen sections may be employed.

Anisotropic substances are physiologically present in visible form in only four organs, namely, the adrenal cortex, thymus, ovary (corpus lutcum) and testis (interstitial cells). Their function has not been determined, but it seems, in the case of the adrenal at least, to be one of importance to the organism.

Pathologically it has been found that anisotropic fatty substances occur only in more or less chronic conditions, and their occurrence is always associated with the actual necrosis of cells. They do not occur in acute diseases (Munk, Kawamura). They are found most frequently in the neighborhood of chronic inflammatory processes, as for example, in the mucosa of the Fallopian tubes in chronic gonorrheal infection, or the gall bladder mucous membrane in chronic cholecystitis. They are commonly found in chronic nephritis. One frequently sees a multitude of small yellow flecks on the surface and in the substance of a cirrhotic kidney, and examined under the polarizing microscope these are found to contain abundant anisotropic fat globules. Amyloid kidneys are especially rich in anisotropic lipins.

Caseous tuberculous areas do not contain anisotropic bodies, but in the neighborhood of such tuberculous foci many small yellow areas filled with doubly refractive substances are often seen. We recently found in the neighborhood of a gangrenous portion of a lung many small deep yellow areas which seemed to occupy alveolar spaces. On examination these were found to be largely composed of desquamated alveolar cells filled with anisotropic substances. The so-called myelin cells found in the sputum in chronic bronchitis, especially chronic influenzal bronchitis, and in catarrhal desquamative pneumonia are alveolar cells and leucocytes filled with anisotropic lipins. Anisotropic lipins are said not to be present in tuberculous salpingitis, whereas their occurrence is quite the rule in gonorrheal salpingitis.

For the sake of completeness, the following conditions may be mentioned in which anisotropic substances have been described: arterio-sclerosis, puerperal uteri, choroid plexus, pyosalpinx, pyometria, purulent membranes, in pyelitis, mesenteric cysts, actinomycosis, chronic mastitis, cholangitis, albuminuric retinitis, xanthoma, the urine and many tumors (carcinoma, sarcoma, hypernephroma, adenoma, etc.).

The anisotropic lipins frequently occur in seemingly intact cells, and are regarded by those most experienced as infiltrations. Cells which are obviously in a condition of necrobiosis often contain anisotropic substances, but we cannot conclude from this that such substances are the result of the decomposition of the containing cells. This would be an indefensible repetition of Virchow's error in regard to fatty degeneration. That anisotropic fats are the result of a vital infiltration and are not the result of protoplasmic degeneration has been shown by the careful chemical work of Windans. He found the amount of cholesterol and of cholesteryl esters far above the normal upon comparing arterio-sclerotic aortas, and kidneys showing chronic nephritis with the normal organs. This can only be interpreted as an infiltration of cholesterol either as such or as an ester, for there is no more proof that cholesterol is derivable from proteins than there is of such an origin for the neutral fats. The problem is the same in both cases. Anisotropic substances may be present in parenchyma cells, as for example those of the convoluted tubules of the kidney; they are found in the endothelial cells of lymph vessels, and occur free in the tissue spaces and lymphatics. Ordinary isotropic neutral fats are almost always mixed with the anisotropic, and usually the former predominate.

What is the source of these peculiar complex lipins, and why are they found only in subacute or chronic conditions associated with the necrobiosis of cells? It is well to admit

at once that answers to these questions are of necessity, at the present time, partially speculative. Much careful chemical and pathological investigation will be required to answer them with certainty. The lipins both simple and complex are, as we know, essential and constant constituents of the cell. They form the covering membranes of the nucleus and cell granules (Albrecht, Faure-Fremict) and have been shown to be most important factors in the osmotic interchanges between the cell and its environment (Meyer, Overton).

Anisotropic lipins are formed very slowly and are in all probability the result of chemical and physical rearrangements of the lipins derived from broken-down cells whose disintegration has been very gradual. They accumulate in adjacent living cells probably as a result of the same factors which are operative in the production of ordinary (glyceryl ester) fatty infiltration. Phagocytosis by both the wandering and fixed cells must also be considered a factor in the assimilation of fatty substances. The cell, itself, then, is one source from which complex lipins may come, and this is probably the explanation of the frequent association of visible deposits of these substances in the neighborhood of necrobiotic processes.

It must also be borne in mind, as Aschoff points out, that the compounds of cholesteryl esters are contained in the blood plasma, and may under certain conditions accumulate in cells. Xanthoma cells are examples of this infiltration from the blood.

Finally there is a fatty change in cells which takes place during autolysis, and which is to be sharply differentiated from the other fatty changes that we have studied. Organs free from microscopically visible fat when allowed to undergo aseptic autolysis show after a time many small refractile granules of a fatty nature (Waldvogel, Dietrich). These have been termed myelin droplets and they are quite different from the fatty substances which appear in cells during life. They are not doubly refractile and yet differ in their solubility and staining reactions from the neutral fats. They stain with neutral red (Albrecht) and this has led to the belief that they are composed in part at least of fatty acids which have been set free from the lipin compounds present in the nucleus and cytoplasm. Here for the first time we meet with intracellular substances of a fatty nature which are clearly of immediate endogenous origin. The process has been termed "myelinic dissociation," and is to be regarded as a molecular decomposition of the cytoplasm, during which the combined fats of the cell become visible. To these fatty substances which appear post mortem in the cell, the purely physical designation "myelin" has been applied. Their exact chemical composition is unknown. One very interesting property of these so-called myelin droplets is that upon the addition of water, they swell into a great variety of bizarre forms. These "myelin figures," as they are called, are not peculiar to post mortem droplets; one can demonstrate them quite beautifully by adding a solution of ammonia to a drop of oleic acid, and observing the edge of contact under the microscope.

Myelin droplets are seen in cells which show the condition of cloudy swelling, and this suggests that in cloudy swelling we may be dealing with an ante mortem autolysis of the cytoplasm. Cloudy swelling could thus be regarded as one of the earliest indications of cellular necrobiosis, and there is much to be said for this view.

To recapitulate:

1. The large group of fatty substances which, following Rosenbloom and Gies, we have called lipins, embraces besides the neutral fats, fatty acids and soaps, a number of more complex substances which occupy a place of great practical importance in the study of the normal and abnormal metabolism of fats.

2. Lipins are constant cell constituents and occur in both visible and invisible forms. The invisible form usually predominates in the healthy cell, but various cell injuries are accompanied by visible accumulations of lipins.

3. Such fatty accumulations are not the result of a degenerative transformation of the cytoplasm into fat, but represent deposits of lipins which, owing to some injury, the cell cannot utilize. The term "fatty degeneration" should be discarded as erroneous and obsolete.

4. All visible accumulations of lipins occurring in living cells are to be regarded as infiltrations, and they may be physiological or pathological.

5. Pathological fatty infiltrations may be divided for purposes of study into

(a) Glyceryl-ester infiltrations.
(b) Cholesteryl-ester infiltrations.
(c) Infiltrations of other lipins.

Glyceryl-ester infiltration indicates an injury to the containing cell, while cholesteryl-ester and other lipin infiltrations are indicative of the necrobiosis of neighboring cells.

6. Cholesteryl-esters assume fluid crystalline, anisotropic forms in the body and the presence of such anisotropic accumulations are characteristic of chronic degenerative lesions.

7. During autolysis, the invisible lipins of the cell assume a visible form, but they differ characteristically from the lipins which are deposited in cells during life. The process is termed myelinic decomposition or dissociation and has no connection with the process of fatty infiltration.

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Detailed references to the literature have been purposely omitted from the text since they are readily available in exhaustive form in the monographs of Leathes, Bang, and Kawamura.

PROFESSOR SAMUEL D. GROSS: AMERICA'S FOREMOST SURGEON.[1]

By C. W. G. Rohrer, M. A., M. D., Ph. D., Baltimore, Md.

It was the late Bishop Phillips Brooks who said: "If I ever wrote a book I would want it to be a biography, portraying a great man's life." To-night I shall make a feeble attempt to outline a life-history of the manner of man indicated by Bishop Brooks.

Birth and Parentage.

Samuel David Gross, the subject of my sketch, was born near Easton, Northampton County, Pennsylvania, on the 8th of July, 1805. The original Gross homestead, about four miles from the city of Easton on the Northampton Pike, was a fine farm embracing two hundred acres of the best land, in a high state of cultivation. Upon it was a large orchard famed for the abundance and excellent quality of its fruit. Besides the other necessary farm buildings, this tract of land was improved by a two and one-half story stone house, a portion of which is still standing. It has long since passed into the hands of strangers, and is now known as "Chesterfield Farm." The old stone house has been remodeled and rebuilt, and is occupied by the gardener. Within its quaint walls Dr. Gross first saw the light of day; from its rude doorway he went forth an humble country lad, to eventually become America's foremost surgeon.

Philip Gross, his father, was a man of sterling worth. He was one of the most highly respected citizens in Eastern Pennsylvania. He was tall, handsome, and of dignified bearing. His son, the Doctor, inherited his father's physical beauty and manly traits. The father died of apoplexy in November, 1813, at the age of fifty-six, when his son was in his ninth year.

Juliana Gross, his mother, was, before her marriage, a Brown; she died of asthma in March, 1853, at the advanced age of eighty-six years. She is described as a woman of lovable character, and an excellent wife and mother. Her son attributes much of his professional success to the training which he received at his mother's knee, and to the influence of her exemplary life. Both parents were of German descent, and natives of Pennsylvania.

Dr. Gross had two sisters and three brothers. One of his brothers, the Rev. Joseph B. Gross, was for many years a well-known clergyman of the Lutheran Church, to which religious sect the Gross family for generations had belonged.

Boyhood and Youth.

His boyhood and youth were pleasantly spent on the farm. Living much of the time out of doors, he early acquired a fondness for natural history. In the eloquent words of a gifted poetess, Gross at a tender age found

> Tongues in trees, books in running brooks,
> Sermons in stones, and good in everything.

The usual sports and amusements incident to country life were also enthusiastically engaged in by him. Target shooting with a "bow-gun," ball playing, pitching quoits, rabbit-snaring, snow-balling, pitching pennies, and hunting bird's nests were favorite forms of amusement, each in due season. He believed that the skill which he acquired in pitching quoits contributed much to his manual dexterity and surgical acumen. As a boy he was excessively fond of fishing. Another favorite amusement with all country boys is fighting bumblebees, wasps, hornets, and yellow-jackets. In this type of sport, though sometimes resulting in all the cardinal symptoms of inflammation, he soon became an acknowledged leader.

His favorite books were the Bible, Aesop's Fables, and Witches of the Hartz Mountains. Like his illustrious fellow-countryman, Benjamin Franklin, he also read various almanacs, volumes of history, geography, and romance.

Before the age of six years he made known to his parents that he wanted to be a physician. This early impulse permeated the very fibre of his being. It came to him like an inspiration, and dominated the entire period of his childhood and youth; nor did it cease its prompting until it had in a measure been fulfilled.

Early Education.

Dr. Gross obtained the first rudiments of his education at a log-cabin school house located nearly a mile from his home. Here the three R's—Reading, 'Riting, and 'Rithmetic—were taught, as well as the simplest rules of spelling. He soon became an apt pupil, and showed signs of good scholarship. Notwithstanding these hopeful indications, his early advantages were but meagre. As a result, his preliminary education was noticeably defective.

However, there still burned within his boyish heart the desire to be a physician. He had now attained to an age where he could see the defect in his common school education. He was industrious, he was ambitious, and he was imbued with a goodly amount of characteristic German thoroughness. At this juncture he set resolutely to work and took up the study of three languages—Latin, German, and English. He also made commendable progress in reading, composition, and arithmetic.

At the age of seventeen he considered himself fitted to begin the study of medicine. In those days it was customary to "read medicine" in the office of a physician, a practice now almost obsolete. Accordingly he entered the office of a country physician. Receiving but little aid, he withdrew from this practitioner's office and tried another. The result was the same, and he again sought a new preceptor. His third attempt proved subsequently to be equally disastrous. This time

[1] Paper read at the meeting of the Johns Hopkins Hospital Historical Club, January 15, 1912.

In the preparation of this paper I have received valuable assistance from the following persons: Dr. Gross's only surviving son—Mr. A. Haller Gross of Langhorne, Pennsylvania; Dr. W. W. Keen, Dr. J. W. Holland, and Mr. Nelson Alexander Chestnutt of Philadelphia; Dr. Edgar M. Green, Miss Swift, and Mr. Reuben Kolb of Easton, Pennsylvania; and last, but by no means least, my photographer, Mr. Harry B. Weaver of this city.

he had applied to Dr. Joseph K. Swift of Easton, a graduate of the University of Pennsylvania. Dr. Swift is characterized as "an eminent physician and surgeon and a highly cultivated gentleman."

For a brief season the current of the would-be medical student's life ran smooth. No angel "troubled the pool." But it was merely the calm which precedes the storm. To use Dr. Gross's own words:

> With the aid of Fyfe's Anatomy and a skeleton, I learned some osteology; but even this was up-hill business, and I at length gave up in despair. I found that my Latin was inadequate, and that I could not understand the technicalities of medicine without some knowledge of Greek. *This was the turning-point in my life.* I had made a great discovery—a knowledge of my ignorance; and with it came a solemn determination to remedy it.

He did not stand alone in his great discovery. His preceptor, Dr. Swift, was not slow in establishing priority by the reply which he made. According to information which I have received from his grandniece, Miss Swift,[2] when Gross, at that time a country boy, communicated his views to his preceptor, the result far exceeded his most sanguine expectations. Dr. Swift paid him anything but a flattering compliment by telling him "to get an education first, and then study medicine."

He met the situation bravely; relinquishing his medical studies for the time being, he entered college. Wilkes-Barre Academy was the school selected, and here he remained for one year. He next attended a classical school in the city of New York. Becoming dissatisfied, he returned at the end of six months to Easton, where, under the tutelage of his former teacher, Mr. Joel Jones,[3] he took up the study of Latin and Greek. By the end of another half year he longed to return to college to complete his classical studies, and so he went to the Lawrenceville High School, in the State of New Jersey, where he rounded out his preparatory education in a satisfactory manner.

Medical Training.

At the age of nineteen years he began in earnest the study of medicine. In his Autobiography, written shortly before his death, Dr. Gross comments upon the difficulty of choosing a profession. He says: "The choice of a profession is one of the greatest perplexities of a young man's life." Not so, however, in his case, for he was determined from his earliest boyhood to study medicine. From its very incipiency he was wide awake to the seriousness of the proposition. He either may have grasped the situation intuitively, and realized that his was the most laborious and most exacting of the three learned professions—divinity, law, and medicine—or, perhaps, he called to mind the saying of Cicero, that, "In no way do men approach nearer the gods than in trying to give health to their fellowmen."

He began again the study of medicine under Dr. Swift at the age of nineteen. He applied himself diligently for nearly a year, at the expiration of which time his health broke down. Accompanied by one of his brothers, he rode to Niagara on horseback to recuperate. At the end of six weeks he was as well as ever, and returned to his studies. In October, 1826, he proceeded to Philadelphia, and immediately enrolled himself as a private pupil of Dr. George McClellan,[4] professor of surgery in Jefferson Medical College, and several weeks later he matriculated at Jefferson Medical College.

Gross was an indefatigable and painstaking student; whatsoever his hand found to do, he did with his might. The medical student of to-day could not do better than copy his example. Concerning his ne'er-to-be-forgotten medical student days he thus writes in his Autobiography:

> I worked early and late, and lost no occasion to profit by the opportunities that were afforded me. I was determined to qualify myself well, especially in the practical branches. I was very fond of anatomy and surgery, and therefore made them objects of particular inquiry. During the eighteen months of my connection with McClellan I had witnessed many important operations, and had seen a good deal of medical practice. My mind, too, was well disciplined; I had not only industry, but ambition; my morals and habits were good, and I was a stranger to all amusements. Medicine was the goddess of my idolatry.

He was graduated from Jefferson Medical College, in the year 1828. He had attended three sessions of the college, and was one of a class of twenty-seven to receive the honors of the doctorate. His graduation thesis was on the Nature and Treatment of Cataract. The commencement address to the graduates was delivered by his preceptor, Dr. McClellan.

Professional Career.

After a short visit to his mother at Easton, Gross returned to Philadelphia, which city he determined to make his future home. He opened an office at the corner of Library and Fifth streets, immediately opposite Independence Square, and announced himself as a candidate for business. As is usually the case with a young physician, especially in a large city, practice came slowly, but he was not idle. He improved his leisure moments by translating four foreign works on medicine and surgery, to which I shall again refer.

After a vain struggle of eighteen months in the "City of Brotherly Love," he found himself in financial straits. His patrimony was exhausted, and the income from his practice scarcely exceeded three hundred dollars. There was but one alternative—to return to Easton, where living expenses were lower and a young physician's opportunities greater. Accordingly, in April, 1830, he returned to Easton to take up the burden of life again amid the scenes of his nativity. Here he gradually acquired practice, and in a year or so he was regarded as a scientific physician. His office was on Centre Square, opposite that of his old preceptor, Dr. Swift.

[2] It is interesting to note that his sign (or "shingle," as we sometimes call it), weather-beaten and old, still adorns the door-panel of Miss Swift's comfortable home in Easton.

[3] Subsequently elected to the judgeship.

[4] Dr. McClellan's life story is soon told: he was great as a medical teacher, great as a surgeon, the founder of Jefferson Medical College, Philadelphia, the preceptor of Dr. Gross, the father of the late General George B. McClellan, and grandfather of ex-mayor McClellan of Greater New York.

Dr. Gross in His Prime.

Portrait of Dr. Gross
in Library of Jefferson Medical College.

The Gross Homestead.

"Within its quaint walls Dr. Gross first saw the light of day; from its rude doorway he went forth an humble country lad, to eventually become America's foremost surgeon."

His interest in practical anatomy never abated one jot. In the rear of his Easton home there was a garden; at its foot he had a small stone building erected, which he used for a dissecting room. A human subject was occasionally procured from Philadelphia, which he himself transported to Easton in a buggy. Numerous unsuspecting cats and dogs also fell a prey to his thirst for anatomical investigation.

The following incident which occurred while he resided in Easton is authentic. It was communicated to me by Dr. Edgar M. Green, a son of the late Dr. Traill Green, and one of the most prominent physicians in Easton. It was also related by Dr. Traill Green himself at the complimentary dinner given to Dr. Gross on April 10, 1879. At the time—it was in the year 1833—Dr. Gross was conducting experiments on dogs and rabbits, to illustrate the subject of manual strangulation. Many a dog was hanged as a martyr to science. A soldier, a drunken, worthless fellow about Easton, had committed suicide by hanging. Some trouble was experienced in getting him decently buried, but finally he was interred in the cemetery at Easton. In the evening of the same day Traill Green, then a student of medicine at the University of Pennsylvania, was out visiting, when Gross called him to the door and said: "Green, I want that fellow." That night at the hour consecrated to evil spirits, ghosts, ghouls, and hobgoblins, Gross, Traill Green, and another student marched to the cemetery. They took with them a wheelbarrow and a spade. The night was still and very dark. As is usually the case with paupers and unclaimed dead, the man had been buried in a remote corner of the potter's field, where the soil was rough and undulating. They immediately set to work to unearth the coffin. They had not proceeded very far, however, before they were forced to desist. The spade made so much noise in the gravel that they were afraid some one would hear them. Gross said: "Green, we had better quit or we'll get caught." So they gave it up, refilled the grave and left. Several days later a brother of the deceased soldier met Traill Green in the street and said: "Doctor, I believe you got my brother's body." Green replied with the evasive answer, "You can believe what you please." Thus the incident was closed.

Gross longed to qualify himself as a teacher of anatomy. In the spring of 1833 he made known his wishes to Dr. John Eberle, one of his old college preceptors, then a professor in the Medical College of Ohio, at Cincinnati. The result was that he was soon appointed Demonstrator of Anatomy in that institution—the Medical College of Ohio. Accordingly in October, 1833, after a residence of three and one-half years in Easton, he removed to Cincinnati, the "Queen City of the West," to assume his anatomical duties there. He held the position for only two sessions, 1833 to 1835. In 1835 the Medical Department of the Cincinnati College was organized, with a chair of Pathological Anatomy, and to this chair he was unanimously appointed by the trustees. Here he delivered the first systematic course of lectures on morbid anatomy ever given in the United States.

In 1839 Gross was appointed Professor of Medicine in the University of Virginia. A short time previously he had been offered the chair of anatomy in the University of Louisiana. Both of these offers were promptly declined, but in the spring of 1840 he accepted the professorship of surgery in the Louisville Medical Institute, afterwards the University of Louisville. In the following October (1840) he removed from Cincinnati to Kentucky, to inaugurate his work as Professor of Surgery in the University of Louisville.[5]

Gross remained at Louisville for sixteen years, from October, 1840, to September, 1856, with the exception of the winter of 1850-1851, which he spent in New York, as the successor of Dr. Valentine Mott in the chair of Surgery in the University of that city. Shortly after the close of the session, Gross left New York and returned to Louisville.

In 1855 Gross was solicited to allow his name to be proposed as a candidate for the chair of Surgery in the University of Pennsylvania. Various reasons, however, induced him to decline this offer. Early in May, 1856, he was unanimously elected Professor of Surgery in the Jefferson Medical College, from which institution he had been graduated at the age of twenty-three years. This call he could not refuse; so, late in September of the same year (1856), he removed with his family to Philadelphia, where he spent the remainder of his life. He succeeded Dr. Thomas Dent Mütter in the faculty of his Alma Mater, and held the chair from 1856 to 1882, a period of twenty-six years.

Books and Publications.

Long before Gross finished his student course of studies in Jefferson Medical College, he had determined to undertake the translation of some French work as soon as he should receive his degree. He already had made a selection of Edwards's Manual of Surgical Anatomy, but a few days before he thought of beginning, he found, much to his chagrin and disappointment, that he had been forestalled in his contem-

[5] The following letter from Dr. E. O. Smith, secretary of the faculty of the Ohio-Miami Medical College of the University of Cincinnati, adds some light to this early history:

Cincinnati, Ohio, January 5, 1912.

Dr. C. W. G. Rohrer, 114 W. Franklin St., Baltimore, Md.

Dear Doctor: Your communication was received yesterday and I have found the following information.

In 1833, through the influence of Dr. John Eberle, Professor of Materia Medica in the Medical College of Ohio, Dr. Samuel D. Gross was appointed demonstrator of Anatomy in that school. In 1835, when Daniel Drake founded the Medical Department of the Cincinnati College, Gross was made Professor of Pathological Anatomy and remained with that school until it closed in 1839. In 1840 he became Professor of Surgery in the Louisville Medical Institute, which position he held for sixteen years. I cannot send you catalogues confirming the above statements as we have no duplicates and the only picture we have of Dr. Gross is framed with a group of other early teachers and of course you can easily see that it would be impossible to send it. However, the statements made are authentic and you can use them in your paper.

Trusting that this is the information that you desire, I am,

Respectfully yours,

(Signed) E. O. Smith,
Secretary of Faculty.

plated task by Mr. Coulson of London. While debating in his own mind what to do next, he had placed in his hands a French work on anatomy—Bayle and Hollard's General Anatomy. Within a year after his graduation he not only translated this book, but also three additional foreign works—Hatin's Manual of Obstetrics, Hildenbrand on Typhus Fever, and Tavernier's Operative Surgery. He completed his first translation, Bayle and Hollard's General Anatomy, in two months. It formed an octavo volume of about three hundred pages, and the edition numbered two thousand copies. The publisher, Mr. John Grigg of Philadelphia, paid him two hundred dollars for it. In the opening paragraph of his preface Gross first comments upon the newness of this branch of anatomy and then pays a tribute to Bichat. He says:

> General Anatomy is a science of comparatively modern date; and, like every other great and important improvement, it has gradually arrived at its present degree of perfection. To Bichat, no doubt, is due the honor of having first established this branch of anatomy into a science, and the work which he has left us upon this subject is at once an imperishable monument of his great talents and of his ingenious and profound researches.[6]

His second translation was another French work—Hatin's Manual of Obstetrics—a small practical treatise of 166 pages and an appendix. The latter, consisting of 18 pages, contains Magendie's celebrated paper on the cephalo-spinal fluid, which was translated by Dr. Joseph Gardner, a fellow-graduate of Gross. This translation was completed in three weeks, and was also published by Mr. Grigg, who paid Gross the munificent sum of seventy-five dollars.

The third work translated by Gross was Hildenbrand on Typhus Fever. At that time typhus fever, variously called "ship fever" or "jail fever," was a deadly and widely prevalent disease. This little German book was much celebrated in its day. The translation was published by Mr. Elam Bliss of New York, in the winter of 1829. The volume of 180 pages was completed in two months and Gross received one hundred and seventy-five dollars for it. It is interesting to observe that 1829, the year it was published, is the year in which Louis of Paris coined the name "typhoid fever."

It is manifestly evident that Hildenbrand, writing in 1809, must have recognized typhoid fever, and described it under the name of nervous or non-contagious fever. His book contains twelve sections or chapters, and he writes, Section I, p. 9:

> It (the contagious typhus) is distinguished from the pure nervous and asthenic fevers, properly so called, in this, that, although these fevers are ushered in with true vital debility and the ordinary nervous symptoms, they are not contagious; and the affected nervous system manifests only some particular signs of this contagion, as for instance, the stupor and some others which we shall hereafter describe when speaking of the course of typhus. The exanthemata, perhaps, also establish some difference, as well as the periodical exacerbations, which are more peculiar to the simple nervous fevers.

Section II is very interesting, and is entitled "On the Antiquity and History of Typhus, and of Its Effects Upon the Human Race."

Section IV is devoted to the contagious typhus. Its full caption is "Of the Simple Regular Typhus, Communicated by Contagion." In contrast to Section IV is Section XII, entitled "General Observations on the Originary Typhus." In Section XII, page 173, the author says:

> It (the originary typhus) is distinguished from the simple nervous and non-contagious fever, in this, that in the latter, the vertiginous stupor and the catharrhal symptoms are completely wanting; while the other symptoms, such as the subsultus tendinum, the convulsions, the cramps and the general erethism of the body, are greatly aggravated. The periodical exacerbations, whether quotidian, or tertian, are likewise more peculiar to the simple nervous and non-contagious fevers.

The fourth translation by Gross, and the last he ever attempted, was another French book, Tavernier's Operative Surgery. The first volume was translated in less than three months. Tavernier's work of two octavo volumes of nearly five hundred pages each, was the first treatise on operative surgery ever published in the United States.[7] The publisher, Mr. Grigg, paid Gross four hundred dollars for his labors. Volume II, entitled Clinical Surgery, was not translated by him.

Before passing from these four translations to his original works, I wish to call brief attention to the rapidity and magnitude of the task accomplished by the young physician. It was his custom to translate from twenty to twenty-five pages a day, no matter what might be his other engagements. The average French or German student of the present generation would be in imminent danger of heart failure if his teacher were to assign him so stupendous a task.

Having completed the four above-mentioned translations, Gross set to work forthwith upon the composition of his first original work. This book, written with a facile pen, was entitled "The Anatomy, Physiology, and Diseases of the Bones and Joints." It consists of an octavo volume of nearly four hundred pages, and was finished in the space of little more than three months. The work was issued in the autumn of 1830, by Mr. Grigg. The preface is dated "Easton, July, 1830."

When he wrote this book he was but twenty-five years of age, and he seems to have had some misgivings as to the reception which would probably be accorded it because of his youth and inexperience. On page iv of the Preface, Gross states:

> "If," to use the language of an eloquent writer,[8] "any one should conceive the present undertaking to be above the capacity

[6] I wish to call attention to the fact that in Bayle and Hollard's General Anatomy each subject closes with a paragraph on pathological anatomy and a complete bibliography. There is also an Appendix, containing an account of four so-called Accidental Tissues: a. Tuberculous productions. b. Scirrhus. c. Encephaloid or cerebriform cancer. d. The melanotic substance.

[7] This surgery is preceded by an Introduction consisting of twenty-five closely printed pages, which gives a concise history of surgery. In Chapter IV, Sec. 4, p. 308, occurs a brief account of Sir Astley Cooper's famous operation of ligating the abdominal aorta.

[8] Richerand. Preface to his Elements of Physiology.

of my age, I will say, even at the risk of a paradox, that young men are perhaps best fitted to compose elementary works; because the difficulties which they have encountered in their studies, as well as the steps which they have taken to overcome them, are still fresh in their memory."

However, this early effort was well received, and two thousand copies were exhausted in less than four years. A second edition was not issued. The author states that he never received a cent of remuneration for this book.

Dr. Gross was the first to describe the use of adhesive plaster in the treatment of fractures. This description (Chap. II, Art. II, under the caption, "Treatment of Complicated Fractures") reads as follows:

If the bone be broken into several pieces, and any of them are completely detached, or so loose as to render their union highly improbable, all such pieces ought to be carefully removed; after which the edges of the wound should be slightly approximated, and kept in this position by a few short strips of adhesive plaster. The limb should be placed upon a pillow and surrounded with the bandage of Scultetus, and every care taken to obviate and remove inflammation. When the wound suppurates, it should be frequently dressed with some digestive ointment, or soft emollient poultices, as circumstances may require, care being taken that at each application of them the fracture be disturbed as little as possible. As soon as the inflammation has subsided, and the parts begin to heal, the ends of the fragments should be brought into contact, and be maintained in apposition by appropriate splints and dressings..... In complicated fractures of the leg, it not unfrequently happens that the soft parts about the ankle are so much contused, or otherwise injured, as to render it impossible to employ the usual extending bands. When this is found to be the case, the difficulty may usually be remedied by applying along each side of the leg, as high up as the seat of the fracture will admit, a piece of strong muslin, about two feet and a half in length, two inches and a half in width, and spread at one of its extremities with adhesive plaster. The part which is applied upon the limb should be confined by three or four circular strips, so as to keep it firmly in its place, and equalize the extending power. The free extremities of the extending bands should then be tied under the sole of the foot, and be secured to the block or bar which connects the lower ends of the splints. This mode of making extension, for which we are indebted to the ingenuity of my friend and preceptor, Dr. Swift, of this place (Easton), will, I am fully persuaded, be found highly useful in practice, and satisfactorily obviate the inconveniences to which I have just alluded.

Apropos of the four translations and the book on the Bones and Joints, Gross thus writes in his Autobiography (p. 43):

All these works were published in about eighteen months after I took my degree. The different translations and the book on the Bones and Joints formed nearly fifteen hundred pages octavo. In addition to this, I assisted the late Dr. Godman in translating the Duke of Saxe-Weimar's Travels in the United States, published soon afterwards by Carey and Lea. This work was written in German, and I completed about two hundred pages of it in less, I think, than a fortnight.... My practice during this period was, of course, limited; I went little into society and took hardly any recreation. Depriving myself of pleasure and amusement, I devoted my time to my task, thus literally verifying the saying of the Roman, *Nulla dies sine linea.* I labored day and night under the stimulus both of ambition and of poverty.

As has been stated in a previous paragraph, in the month of April, 1830, Gross removed from Philadelphia to Easton. While residing there he spent all his leisure during the summer months upon the composition of a work on Descriptive Anatomy. In it he makes the effort for the first time in English to change the nomenclature of anatomy from Latin into English. This book, however, was never entirely completed and never published.

Next, as a result of four years' study and teaching, his Elements of Pathological Anatomy was published. The work was founded upon knowledge derived from dissections made during his occupancy of the chair of pathological anatomy in the Cincinnati Medical College, from an elaborate course of reading, and from numerous visits to the slaughter-houses of Cincinnati. It was issued in 1839, in two octavo volumes of more than five hundred pages each. The book was illustrated by numerous wood-cuts and several colored engravings, and was the first systematic work upon the subject ever published in the United States, or, indeed, in the English language.

It is true, as the worthy president of this society, Dr. Henry Barton Jacobs, told us in his interesting disquisition on "The Gold-headed Cane," that Dr. Matthew Baillie of London published a little book on pathology as early as 1793, but Dr. Baillie's book does not purport to be a complete treatise. It is entitled, "On the Morbid Anatomy of Some of the Most Important Parts of the Human Body."

In Volume II (pp. 458-463), Gross gives an account of a number of dissections of specimens of false conceptions or uterine moles—the first account of them in the English language. His examinations of the prostate gland have also been fully quoted by Sir Henry Thompson and others.

A second edition of the Elements of Pathological Anatomy, greatly enlarged and thoroughly revised, was issued in 1845. It consists of one large octavo volume of eight hundred and twenty-two pages, illustrated by colored engravings and two hundred and fifty wood-cuts. It contains full marginal references, which greatly enhance its value. A copy of the second edition was a favorite book of Professor Rudolph Virchow. Speaking of the Elements, Dr. J. M. DaCosta, in his Biographical Sketch of Dr. Gross, says:

It is a mine of learning, and its extended references make it valuable to this day. Its merits have been fully recognized abroad; and on no occasion more flatteringly than when the great pathologist, Virchow, at a dinner given to Dr. Gross at Berlin in 1868, complimented him publically on being the author, and, pointing to the volume, which he laid upon the table, gracefully acknowledged the pleasure and instruction which he had often gained from it.

A third and last edition of this work appeared in 1857, from the press of Blanchard and Lea. It was in some degree an abridgment of the second edition, and yet it comprised a very good outline of the existing state of the science.

Before leaving the subject of pathological anatomy and passing on to the next, I wish to quote a few sentences relating thereto, written by Gross in February, 1870, as follows:

A knowledge of pathological anatomy is the very basis of diagnosis; and when it is considered how important it is that a physician should be able to determine the nature of a disease before he institutes his treatment, it is not a little surprising that this

department of medicine should be taught in so few of our medical schools. This omission is one of the crying sins of the present day. Everything, however irrelevant and useless, is taught to the exclusion of morbid anatomy. I only wish that every medical college in the country were compelled to introduce it into its curriculum of studies. To make room for it we might well dispense with some of the useless teachings in chemistry, materia medica, physiology, and even midwifery, so characteristic of the present day.

In 1842 Dr. Gross edited, with copious notes and additions, the American publication of Robert Liston's Elements of Surgery, a famous work in its day. Liston's book had a perfect right to be good, because its author was ably seconded in his anatomical and surgical investigations by one Ben Crouch—probably the most celebrated resurrectionist or body-snatcher of all time.

In the spring of 1841, Dr. Gross commenced his investigations on the nature and treatment of wounds of the intestines. The experiments, upwards of seventy in number, were performed exclusively on dogs, and were continued with various intermissions for more than two years, culminating in the publication, in 1843, of a work entitled, "Wounds of the Intestines."

Blanchard and Lea, in 1851, published his work entitled, "A Practical Treatise on the Diseases, Injuries and Malformations of the Urinary Bladder, the Prostate Gland, and the Urethra." This work was at once accepted as authoritative upon these subjects. A second edition, greatly enlarged and improved, was issued in 1855. It forms a closely-printed octavo volume of nine hundred and twenty-five pages, illustrated by one hundred and eighty-four wood-cuts. Perhaps the best-known of these wood-cuts are those (pp. 70 and 71) illustrating the size and form of the human prostate gland in seven subjects of different ages. In an appendix of twenty-nine closely-printed pages is the first and only attempt ever made by any writer to furnish a complete account of the prevalence of stone in the bladder and of calculous disorders in the United States, Canada, Nova Scotia, Europe, and other countries. A third and last edition of this work was issued in September, 1876, under the able editorship of Dr. Gross's son, Dr. Samuel W. Gross.

In 1854, Dr. Gross's work, "A Practical Treatise on Foreign Bodies in the Air-Passages," was also issued from the press of Blanchard and Lea. He was occupied upwards of two years in its composition. It consists of an octavo volume of four hundred and sixty-eight pages, illustrated by fifty-nine engravings on wood. As the author himself states: "It was the first attempt to systematize our knowledge upon the subject, and the work is therefore, strictly speaking, a pioneer work." This work has long been out of print, and has never been reissued. The late Sir Morrell Mackenzie, the highest authority on the subject in Europe, in speaking of this work nearly thirty years after its publication, makes the following remark: "This invaluable essay gives full reports of two hundred cases, and is so complete that it is doubtful whether it will ever be improved upon; indeed, the excellent articles of Bourdillat and Kühn, subsequently published, the former based on three hundred, and the latter on three hundred and seventy-four cases, only confirm the conclusions previously arrived at by Gross."[9]

Several years before Dr. Gross left Kentucky he had commenced the composition of his System of Surgery. He states that he had determined to do his best to make it, if possible, the most elaborate if not the most complete treatise in the English language. Early in the spring of 1859 the manuscript was submitted to the publishers, Messrs. Blanchard and Lea. The preface is dated Jefferson Medical College, Philadelphia, July 8, 1859. The work consists of two portly octavo volumes, numbering in the aggregate two thousand three hundred and sixty pages, and illustrated by nine hundred and thirty-six engravings on wood. The edition comprised two thousand copies. The full title of the work is:

A
SYSTEM OF SURGERY;
PATHOLOGICAL, DIAGNOSTIC, THERAPEUTIC,
AND OPERATIVE.
BY
SAMUEL D. GROSS, M. D.,
Professor of Surgery in the Jefferson Medical College of Philadelphia;
Member of the American Philosophical Society; Fellow of the College of Physicians of Philadelphia;
Corresponding Member of the New York Academy of Medicine, and of the
Imperial Royal Medical Society of Vienna;
Author of a Treatise on the Urinary Organs, etc.
ILLUSTRATED BY
NINE HUNDRED AND THIRTY-SIX ENGRAVINGS.
IN TWO VOLUMES.
PHILADELPHIA:
BLANCHARD AND LEA.
1859.

The following inscription adorns the dedicatory page of Dr. Gross's System of Surgery:

TO
THE NUMEROUS PUPILS
WHO, DURING THE LAST QUARTER OF A CENTURY,
HAVE ATTENDED HIS LECTURES,
AND WHO ARE NOW SETTLED IN EVERY SECTION OF THE UNITED STATES
IN THE
HONORABLE PURSUIT OF THEIR PROFESSION,
THESE VOLUMES,
DESIGNED TO ILLUSTRATE ONE OF THE MOST IMPORTANT AND VALUABLE BRANCHES OF THE HEALING ART,
ARE RESPECTFULLY AND AFFECTIONATELY INSCRIBED
BY THEIR FRIEND,
THE AUTHOR.

The comprehensiveness of this system is indicated in one sentence on the first page of the preface. Dr. Gross writes:

[9] Sir Morrell Mackenzie: Diseases of the Throat and Nose, vol. I, p. 450. Philadelphia, 1880.

"My aim has been to embrace the whole domain of surgery, and to allot to every subject its legitimate claim to notice in the great family of external diseases and accidents."

In Volume I (pp. 588-589), he discourses eloquently on the "Qualifications of a Surgeon." The four paragraphs could be read with advantage by every medical student. He sums up the situation as follows:

> Celsus, long ago, happily defined the qualities which constitute a good operator. He should possess, says the illustrious Roman, a firm and steady hand, a keen eye, and the most unflinching courage, which can disregard alike the sight of blood and the cries of the patient.

Some of us, I am sure, are also reminded of Sir John Bell's ideal of the qualities necessary in a truly great surgeon—"The brain of an Apollo, the heart of a lion, the eye of an eagle, and the hand of a woman."

The Gross System of Surgery passed through six editions, each being a decided improvement upon its predecessor. The sixth and last edition was issued in 1882, just seventeen months before the death of its venerable author.

At the outbreak of the Civil War, Dr. Gross wrote a brief Manual of Military Surgery. It was composed in nine days, and published in a fortnight from the time of its inception. Under the care of Messrs. J. B. Lippincott and Company, it passed through two editions of 2,000 copies each. It was republished at Richmond, Virginia, and was extensively used by the surgeons of both armies. In 1874, it was translated into Japanese and published at Tokio, Japan. The first edition bears the date of 1861; the second edition, 1862.[10]

In 1861 Dr. Gross wrote, or rather edited, a work entitled, "Lives of Eminent American Physicians and Surgeons of the Nineteenth Century." It is an octavo volume of upwards of eight hundred pages, now exceedingly scarce. To this work he contributed three sketches on Dr. Ephraim McDowell, Dr. Daniel Drake, and Dr. John Syng Dorsey. This book is the third publication on American medical biography. The first, issued in 1828, was edited by Dr. James Thacher of Massachusetts, and the second, edited by the late Dr. Stephen W. Williams, also of Massachusetts, appeared in 1845. Dr. Gross's book contains a full and complete account of the life and work of thirty-two eminent American physicians and surgeons, now of a by-gone medical epoch.

A few years later he wrote a valuable work entitled, "A Full Account of Special Surgery on Diseases and Injuries of Particular Organs, Textures, and Regions." A fifth edition of this work was issued in 1872.

In 1876 he wrote the section on Surgery, in the centennial volume entitled, "A Century of American Medicine, 1776-1876." It is a masterly article consisting of one hundred pages, originally contributed to The American Journal of the Medical Sciences.

Dr. Gross delivered the first anniversary address before the Philadelphia Academy of Surgery in 1881. It was a memoir of John Hunter, with the title of John Hunter and His Pupils, later published in book form. In the preface he states: "In assuming this duty I selected for my theme the life, character, and services of the founder of scientific surgery." The portrait which fronts this little volume on John Hunter is the familiar one from Sharp's steel engraving of Sir Joshua Reynold's celebrated painting. The text itself has been liberally quoted by Dr. Mather, in his excellent book entitled, "Two Great Scotsmen—William and John Hunter."

On February 14, 1884, Dr. Gross made the final entry in his Autobiography, a handsome two-volume work which has come down to us as a priceless heritage. The Autobiography was edited by his two sons—the late Dr. Samuel W. Gross and the Hon. A. Haller Gross of the Philadelphia Bar. Its full title is: "Autobiography of Samuel D. Gross, M. D., with Reminiscences of his Times and Contemporaries." It was begun about fifteen years prior to the death of its distinguished author and published in 1887, three years subsequently. In the opening paragraph, Dr. Gross states his reasons for writing it in the following words:

> It is my wish to write a sketch of my life for the gratification of my children and grandchildren, and for the benefit of such members of my profession as may feel an interest in me from my long connection with it. Possibly some good may grow out of such a labor, by stimulating the ambition of those who may come after me to work for the advancement of science and the amelioration of human suffering. The devotion which I have shown to my profession may, perhaps, exert a salutary influence upon the conduct of young physicians, and thus serve to inspire them with a desire to excel in good deeds.

The Autobiography is preceded by a Memoir of Dr. Gross by the late Dr. Austin Flint, Sr., a former colleague and lifelong friend. This Memoir is an excellent portrayal of the life and labors of one of the foremost men of his day—one who is declared to have been "perhaps the most eminent exponent of medical science that America has yet produced."

Contributions to Medical Science.

In addition to his published works, Dr. Gross wrote numerous important journal articles, which cover a wide range of subjects. The principal titles, arranged in chronological order, are as follows:

Report on Kentucky Surgery, 1851.

An Account of a Case of Axillary Aneurism, 1852.

On the Diseases and Operations on the Jaws, 1852.

A Short Account of the Use of Adhesive Plaster in the Treatment of Fractures, 1852.

A Discourse upon the Life and Character of the late Dr. Drake, 1853.

Results of Surgical Operations in Malignant Diseases, 1853.

Causes which Retard the Progress of American Medical Literature, 1856.

August Gottlieb Richter: his Works and his Contemporaries, 1856.

Hypertrophy of the Gums, 1856.

Report of a Case of Gunshot Wound of the Neck, 1856.

Necrological Notice of the late Dr. John K. Mitchell, 1858.

[10] Another favorite volume with the surgeons of both contending armies was Dr. Julian J. Chisolm's excellent "Manual of Military Surgery for the Use of Surgeons in the Confederate Army, 1861."

Nature and Treatment of Tuberculosis of the Hip-joint, 1858.
Sketch of the Life and Services of Ambroise Paré, 1860.
An Account of a Remarkable Case of Melanosis, or Black Cancer, 1860.
Practical Observations on the Nature and Treatment of Prostatorrhoea, 1860.
Brunonianism, Toddism, and other Isms, 1861.
Necrological Notice of Jedediah Cobb, M. D., 1861.
Biographical Sketch of Charles Wilkins Short, M. D., 1865.
Then and Now: Advances in Medical Science in the Past Forty Years, 1867.
The Live Physician, 1868.
A Memoir of Valentine Mott, M. D., 1868.
A New Method of Appointing Medical Witnesses as Experts in Cases involving Medico-Legal Considerations, 1868.
A Memoir of Robley Dunglison, M. D., 1869.
Training of Nurses, 1869.
Nature's Voice in Disease and Convalescence, 1870.
Syphilis in its Relation to the National Health, 1874.
The Factors of Disease and Death after Injuries, Parturition, and Surgical Operations, 1874.
Bloodletting Considered as a Therapeutic Agent; or, One of the Lost Arts, 1875.
The Glories and Hardships of the Medical Life, 1875.
The Proximate Cause of Pain, 1877.
A Memoir of Dr. Isaac Hays, 1879.
The Social Position of the Doctor, 1880.
Value of Early Operations in Morbid Growths, 1883.
The Importance of Having Trained Nurses for the Smaller Towns and Rural Districts, and the Proper Method of Securing Them, 1883.
Obituary Notice of Dr. J. Marion Sims, 1883.
Wounds of the Intestines, 1884.
Lacerations of the Female Sexual Organs Consequent upon Parturition, 1884.

I cannot attempt to describe all of these thirty-seven papers and journal articles, but two or three notes may add to their interest. For example, it was in his elaborate "Report on Kentucky Surgery," prepared in 1851, that Dr. Gross first established the fact that the late Dr. Ephraim McDowell of Danville, in that State, was justly entitled to the honor of being the father of ovariotomy.

In the closing paragraph of his paper on the "Causes which Retard the Progress of American Medical Literature," read before the American Medical Association in 1856, Dr. Gross embodied three resolutions:

Resolved, That this Association earnestly and respectfully recommend, first, the universal adoption, whenever practicable, by our schools, of American works as text-books for their pupils; secondly, the discontinuance of the practice of editing foreign writings; thirdly, a more independent course of the medical periodical press towards foreign productions, and a more liberal one towards American; and, fourthly, a better and more efficient employment of the facts which are continually furnished by our public institutions for the elucidation of the nature of diseases and accidents, and, indirectly, for the formation of an original, a vigorous, and an independent national medical literature.

Resolved, That we venerate the writings of the great medical men, past and present, of our country, and that we consider them as an important element of our professional and national glory.

Resolved, That we shall always hail with pleasure any useful and valuable works emanating from the English press, and that we shall always extend to them a cordial welcome as books of reference, to acquaint us with the progress of legitimate medicine abroad, and to enlighten us in regard to any new facts of which they may be the repositories.

Dr. Gross also gave a number of special lectures and addresses, each being a model of its kind. These may be summarized as follows:

Inaugural Address, Jefferson Medical College, 1856.
Valedictory Address, Jefferson Medical College, 1860.
Address before the Alumni Association, Jefferson Medical College, 1871.
Address before the Medical Society of the State of Pennsylvania, 1871.
History of American Medical Literature from 1776 to the Present Time, 1875.
Address delivered before the Kentucky State Medical Society, 1879.
Valedictory Address, Bellevue Hospital Medical College, 1882.
Address of Welcome before the National Association for the Protection of the Insane and the Prevention of Insanity, 1883.

His Inaugural Address delivered at the opening of the 1856-1857 session of the Jefferson Medical College was a praiseworthy effort. In it he feelingly refers to his regret at leaving Kentucky. He says:

It was pleasant to dwell in the land of Boone, of Clay, and of Crittenden; to behold its fertile fields, its majestic forests, and its beautiful streams; and to associate with its refined, cultivated, generous-hearted, and chivalric people. It was there that I had hoped to spend the remainder of my days upon objects calculated to promote the honor and welfare of its noble profession, and finally to mingle my dust with the dust and ashes of the sons and daughters of Kentucky. But destiny has decreed otherwise. A change has come over my life. I stand this evening in the presence of a new people, a stranger in a strange place, and a candidate for new favors.

He concludes his address in the following words:

Whatever of life, and of health, and of strength remains to me, I hereby, in the presence of Almighty God and of this large assemblage, dedicate to the cause of my Alma Mater, to the interests of Medical Science, and to the good of my fellow-creatures.

I shall pass in brief review but one other of these eight lectures and addresses. It is the address delivered before the Kentucky State Medical Society at its meeting at Danville, May 14, 1879, at the dedication of the monument erected in memory of Ephraim McDowell, the "Father of Ovariotomy." [11] It was a masterly effort, Dr. Gross being at his best.

At the close of the dedicatory services the door-knocker of Dr. McDowell's house was presented to Dr. Gross by Dr. Richard O. Cowling, president of the Kentucky State Medical Society. In presenting it, Dr. Cowling said, in part:

I would that the magician's wand were granted me awhile to weave a fitting legend around this door-knocker, which comes from McDowell to you, Dr. Gross. There is much in the emblem. No one knows better than you how good and how great was the man of whom it speaks. It will tell of many a summons upon

[11] This splendid dedicatory address is given in full in Mrs. Ridenbaugh's excellent Biography of Dr. Ephraim McDowell. It fills sixty-five pages of the book.

mercy's mission which did not sound in vain. Ofttimes has it roused to action one whose deeds have filled the world with fame. A sentinel, it stood at the doorway of a happy and an honorable home, whose master, as he had bravely answered its signals to duty here below, so when the greater summons came, as trustfully answered that, and laid down a stainless life.

It belongs by right to you, Dr. Gross. This household genius passes most fittingly from the dearest of Kentucky's dead surgeons to the most beloved of her living sons in medicine. She will ever claim you as her son, and will look with jealous eye upon those who would wean you from her dear affection.

And as this emblem which now is given to you hangs no longer in a Kentucky doorway, by this token you shall know that all Kentucky doorways are open at your approach. By the relief your skill has wrought; by the griefs your great heart has healed; by the sunshine you have thrown across her threshold; by the honor your fame has brought her; by the fountains of your wisdom at which your loving children within her borders have drunk, the people of Kentucky shall ever open to you their hearts and homes.

Dr. Gross was much overcome by this mark of approbation, coming from the Kentucky State Medical Society, and by Dr. Cowling's well-chosen words. He replied, in part:

I take this emblem now offered to me as the most valued gift of my life. It shall be received into my home as a household god, environed by all the memories of goodness and greatness to which your speaker has referred, and above all recalling this scene. Dying I shall bequeath it, among my most important possessions, to the family that I may leave, or in failure of that, to be preserved in the archives of some society.

Five years later, when Dr. Gross died, Dr. McDowell's door-knocker was presented to the Philadelphia Academy of Surgery. It was subsequently transferred to the museum of the College of Physicians of Philadelphia, where it is now tenderly treasured.

I made an honest effort to borrow Dr. McDowell's door-knocker and bring it to Baltimore, to show at this meeting; but I did not succeed.[12]

Achievements in Medicine and Surgery.

A faithful record of the achievements of Dr. Gross in medicine and surgery would carry us far beyond the limits of the present paper. He usually spoke of himself as a physician rather than a surgeon. His most important original contributions to medicine and surgery, apart from authorship, may thus be enumerated:

Eperiments on dogs and rabbits, to illustrate the subject of manual strangulation.

Experiments upon secretion, to ascertain the rapid transit of certain articles, when taken into the stomach, through the blood by the kidneys.

Weights and measurements of healthy organs.

Experiments on the nature and treatment of wounds of the intestines.

Dissections of specimens of false conceptions, or uterine moles.

Observations on the temperature of venous blood in healthy persons of both sexes.

Deep stitches in wounds of the wall of the abdomen, to prevent hernia or protrusion of the bowel after recovery.

The invention of an enterotome for the treatment of artificial anus.

A tracheotomy forceps, for the extraction of foreign bodies from the air-passages.

Wiring the ends of the bones in dislocations of the sterno-clavicular and acromio-clavicular joints.

Blood catheter, an instrument for drawing off the urine, when mixed with blood.

An arterial compressor—a peculiar pair of forceps—for arresting hemorrhage in deep-seated vessels.

A tourniquet, or compressor, for compressing the vessels of the extremities in amputation.

An instrument for extracting foreign bodies from the nose and ear, found in nearly every pocket case in the country.

Modification of Pirogoff's amputation at the ankle joint, unjustly ascribed to Dr. Quimby, of Jersey City.

Laparotomy in rupture of the bladder.

Direct operation for hernia by suturing the pillars of the ring.

Mode of operating for inverted toe-nail.

Apparatus for the transfusion of blood.

First account of prostatorrhoea.

Description of a new form of neuralgia of the jaws in old persons.

Pododynia, a disease of the foot, first described by him.

He was the first to describe the use of adhesive plaster as a means of making extension in the treatment of fractures of the lower extremity.

He was the first to make it a practice to administer morphine and quinine in large doses.

He was the first to suggest the use of ergot in the treatment of diabetes.

He suggested a new method of treating ganglia of the hand and foot by subcutaneous division of the cyst.

He was the first to practice putting a patient under the full influence of opium, immediately after evacuating a chronic abscess.

He early taught the doctrine of the inflammatory origin and vitality of tubercle of the lungs and other structures.

He was the first to teach that amputation in senile gangrene should be performed at a great distance from the affected parts.

He was the first to sew together the ends of an accidentally divided tendon of the hand.

For many years he taught that scrofulous diseases are nothing but remote forms of syphilis. To-day, however, scrofula is known to be tuberculous in character.

Miscellaneous.

Among his other services to the profession and to humanity at large, the following are deserving of mention. While residing at Easton, in 1832, the great scourge of epidemic Asiatic cholera visited the United States. The disease first appeared in Canada, and then in New York. Early in July it broke out with great virulence in New York City. Great excitement prevailed throughout the entire Atlantic seaboard. Easton, only eighty miles off, participated in the alarm. At a meeting of the town council held on the 19th of July, 1832, Dr. Gross was appointed to visit New York for the purpose of investigating the disease. The situation was one well calcu-

[12] The following note from Dr. Keen explains the situation.

1729 Chestnut Street, Philadelphia,
January 2, 1912.

My Dear Dr. Rohrer: I have your letter of the 1st. Dr. Ephraim McDowell's door-knocker is in the Museum of the College of Physicians. I presume that your photographer would be allowed to photograph it, but no permission I am sure would be granted to take this relic out of the Museum itself.

Yours very truly,
(Signed) W. W. Keen.

lated to try the mettle of the young physician. But he responded heroically to the call of duty and of humanity. I shall repeat briefly the whole story, in the language of Dr. W. W. Keen:[13]

> In 1832, that most dreaded of all scourges, Asiatic cholera, for the first time broke out all over this country with the greatest virulence. Easton was only eighty miles from New York and the citizens, in terror lest the dread disease would reach their own town, appointed a young, intrepid surgeon to visit New York and learn what he could do for their benefit. When others were fleeing in frightened thousands from the pestilence, Gross bravely went directly into the very midst of it, reaching New York when the epidemic was at its very height. In that, then small and half-depopulated, town 385 persons died on the very day of his arrival —and he stayed there a week in a hot July, visiting only its hospitals and its charnel-houses. What call you that but the highest type of bravery?—a bravery which Norfolk and Mobile and Memphis and New Orleans have since seen repeated by scores of courageous physicians ready to sacrifice their lives for their fellow-men with no blare of trumpets, no roar of cannon, no cheer of troops, no plaudits of the press! No battlefield ever saw greater heroes; no country, braver men!

Dr. Gross possessed great powers of organization. He was one of the founders of the Kentucky State Medical Society, and of the Medical Jurisprudence Society of Philadelphia. In the autumn of 1857 he founded, along with Dr. J. M. Da Costa, the Philadelphia Pathological Society. He was the originator of the Philadelphia Academy of Surgery, which was founded in 1879; also the American Surgical Association, instituted in 1880. For this reason we speak of him as the "father of the American Surgical Association," just as we speak of the late Dr. Nathan Smith Davis as the "father of the American Medical Association."

Degrees and Honors.

In addition to the M. D. degree, which Dr. Gross received from Jefferson Medical College in March, 1828, and certificates of proficiency from the several preparatory schools in which he received his academic training, he was the recipient of several honorary degrees from universities at home and abroad. He was made an LL. D. by the Jefferson College of Canonsburg, Pennsylvania, in 1861. In 1872 the University of Oxford conferred upon him the degree of D. C. L., the University of Cambridge the degree of LL. D., in 1880, and the University of Edinburgh and the University of Pennsylvania conferred the same degree, *in absentia,* in April and May, 1884.

He was a member of a score of American medical and scientific societies, and honorary member of nearly a dozen similar European societies. These include honorary membership in the Pathological Society of London, a justly deserved honor, as Dr. Gross was the first regular teacher of pathological anatomy in the United States.

Private Life.

In private life no man was more beloved, whether in his ideal and hospitable home or in the ever-widening circle of his friends and acquaintances. To quote the language of Dr. Austin Flint, Sr.:[14]

> His home was open to all who had any claim upon his attentions. He was considerate and generous alike to the guest who was renowned in letters at home and abroad, and to the young physician and the medical student. As has been said by Froude, "Nowhere is a man known better than in his own family. No disguise is possible there; and he whom father and mother, brother and sister love, we may be sure has deserved to be loved." No father was ever kinder, no husband more affectionate.

Dr. Gross believed in early marriages. True to his convictions, in the winter of 1828-29, in Philadelphia, he married the woman of his choice, the widow of Mr. Hugh Dulany. Her maiden name was Louisa Ann Weissell. She was born in Kensington, London, when her parents were on a visit to England. Mrs. Gross had a singularly gifted intellect and was a most brilliant conversationalist. She was of deep religious convictions. She died February 27, 1876.

Of the eight children born to Dr. and Mrs. Gross, three daughters and five sons, three died in infancy and another in her ninth year. The remaining four attained to their majority. These were two daughters and two sons. One son, the late Dr. Samuel Weissell Gross, whom his father declared to be the "greatest of all his works," died of pneumonia on the 16th of April, 1889, in the fulness of his powers as a great surgeon. At the time of his death he held the chair of Principles of Surgery and Clinical Surgery at the Jefferson Medical College, Philadelphia, and was most signally following in the footsteps of his father, for whose great System of Surgery he was engaged in collecting the information for a projected new edition. A daughter, Louisa, the late Mrs. Benjamin F. Horwitz of this city, a brilliant, charming woman and a great musician, died June 1, 1907.

Two of the children of Dr. Gross are still living. They are Mrs. Maria Gross Horwitz, widow of the late Orville Horwitz, and the Hon. A. Haller Gross, of the Philadelphia bar. To the latter I am indebted for many important facts concerning his father's life, and for the handsome autograph portrait. The traits that stand out in Dr. Gross's life were his purity of character, his great decision, his untiring industry, his self-reliance, his freedom from bigotry and superstition, and his manliness. He was a representative man and citizen. Physically, he was a singularly handsome man, six feet two inches in height, weighing 205 pounds.

Summary of Life Work.

In summing up his life-work, we find that it was great in deeds and also great in years. Born in humble circumstances, his early days were spent in a rural community. Constant outdoor exercise, an excellent home training and example, and a wholesome environment enabled the country lad to lay the foundations of that splendid physique which stood him in such good stead when the responsibilities of a most exacting profession weighed so heavily upon his shoulders. From his youth up he was of studious habits and fond of natural history. He was known as a good, moral young man.

[13] Address at the unveiling of the bronze statue of the late Prof. Samuel D. Gross, M. D., May 5, 1897.

[14] Memoir of Dr. Gross, which precedes the Autobiography, pp. XXVIII-XXIX.

As a medical student, both in the private office and in the medical school, he was ever attentive and diligent, earnestly seeking to make the most of his opportunities. He was primarily a pathologist, secondarily a physician and surgeon. He was a living embodiment of the late Hughlings Jackson's statement, "A good physician must be a good pathologist." And as all operators do who achieve real greatness, he entered the surgical arena through the portals of pathology. He was America's first pathologist.

Dr. Gross always thought himself a better physician than surgeon. As a practitioner, he was very successful, and for many years he had an immense family practice. A large share of his consultation work in Philadelphia, Louisville, and Cincinnati was of a strictly medical character. At one time he was extensively engaged in midwifery in connection with family practice. As an accoucheur he never lost but one woman by puerperal fever, and he never had occasion to apply forceps in any case originally under his care.

As a surgeon, Dr. Gross was a conservative and safe operator. Early in his career he was appalled at the sight of blood. But he possessed the staying qualities of a good operator—a steady hand, an unflinching eye, perfect self-control, and a thorough knowledge of relative anatomy. He was also a skillful diagnostician.

He was an original thinker, an inspiring teacher, and a voluminous author. He was an investigator of the highest rank. In the phraseology of Dr. W. W. Keen: "He 'blazed' more than one new 'trail' in the forests of surgical ignorance."

Closing Years.

On April 10, 1879, a complimentary banquet was given to him at the old St. George Hotel in Philadelphia. It was on the occasion of the fifty-first anniversary of his entrance into the medical profession. It was a memorable gathering, and reference was made to it in the "Remarks of A. Haller Gross at Mr. Potter's[15] luncheon, June 6, 1910," in the following words:

> How well do I recall the occasion, graced as it was by the presence of some of the most distinguished physicians and surgeons of America, who vied one with another in doing honor to my father, and whose burning, eloquent words of welcome and God-speed fill my memory now after the lapse of thirty-one years. I can see Dr. Agnew, the distinguished Professor of Surgery at the University of Pennsylvania, who presided, pinning to the lapel of my father's coat a jeweled badge, presented by the subscribers to the banquet as a testimonial of their affection and esteem, accompanying the act by an exquisite burst of eloquence. And I can recall, as if it were yesterday, a sentence of my father's address—"Oh, for a glance at the profession half a century hence when man, enlightened and refined by education and redeemed from the thraldom of ignorance and superstition, shall reflect more perfectly than he now does the image of his Maker!"

On March 28, 1882, Dr. Gross resigned the chair of surgery in the Jefferson Medical College of Philadelphia, a position which he had filled with signal honor for twenty-six years. Altogether he had been a teacher of medicine and surgery for forty-nine years. His successors to the chair of surgery were his son, Dr. Samuel W. Gross, and Dr. John H. Brinton.[16]

After two years of retirement and failing health, he died, May 6, 1884, at which date he had almost rounded out his seventy-ninth year. A post-mortem examination, conducted by Dr. J. M. Da Costa, showed that Dr. Gross had suffered from marked gastric catarrh. There were irregular thickenings of the mucous membrane of the stomach, and a fatty heart. The right kidney contained a large cyst. The brain weighed forty-eight ounces.

At his own request his body was cremated at Washington, Pennsylvania, in Dr. Lemoyne's crematory, the only one in America at the time. This took place on the 8th of May, and in a little less than two hours and a half all that remained of the "Nestor of American Surgery" were the accustomed seven pounds of ashes. These were placed in an urn, and deposited in Woodlands Cemetery, Philadelphia, next to the coffin of his wife. Upon the urn is the following inscription, written by a former pupil, Dr. D. W. Yandell of Kentucky:

IN MEMORIAM.
WITHIN THIS URN LIE THE ASHES OF
SAMUEL D. GROSS,
A MASTER IN SURGERY.
His life, which neared the extreme limits of the Psalmist, was one unbroken process of laborious years.
He filled chairs in four Medical Colleges in as many States of the Union and added lustre to them all.
He recast Surgical Science, as taught in North America, formulated anew its principles, enlarged its domain, added to its art, and imparted fresh impetus to its study.
He composed many books, and among them

A System of Surgery,

Which is read in different tongues, wherever the Healing Art is practised.
With a great intellect, carefully trained and balanced, he aimed with undivided zeal at the noble end of lessening human suffering and lengthening human life, and so rose to the highest position yet attained in Science by any of his countrymen.
Resolute in truth, he had no fear; yet he was both tolerant and charitable.
Living in enlightened fellowship with all laborers in the world of Science, he was greatly honored by the learned in foreign lands, and deeply loved at home.

Behind the veil of this life there is a mystery which he penetrated on the

SIXTH DAY OF MAY, 1884.

HIS MEMORY

Shall exhort and his Example shall encourage and persuade those who come after him to emulate deeds which, great in themselves, were all crowned by the milk-white flower of

A STAINLESS LIFE.

[15] Hon. William Potter, president of the Board of Trustees of Jefferson Medical College, and at one time United States Minister to Italy.

[16] On June 6, 1910, The Samuel D. Gross Professorship of Surgery was endowed at Jefferson Medical College by his daughter, Mrs. Maria Gross Horwitz, who gave $60,000 for the purpose. Dr. J. Chalmers Da Costa was appointed to the chair.

America has been slow to honor her illustrious dead of the medical profession. Of the fifty-one names in the Hall of Fame, New York University, only one—that of Dr. Oliver Wendell Holmes, is the name of a physician. But Dr. Holmes's name is there, not because of his distinguished professional ability; not because he coined the word "anaesthesia"; not because he was the first to recognize the contagiousness of puerperal fever, but by reason of his eminent literary genius.

Be this as it may, the great surgeon whose name and fame constitute the theme of this evening's meeting was not destined to go down to his grave "unwept, unhonored, and unsung." In the city of Washington, D. C., under the very dome of the capitol of one of the mightiest nations on the face of the globe, there stands a fitting monument to him, in enduring bronze. A loving medical profession presented the statue, which is of heroic size, and the Congress of the United States appropriated $1500 for the pedestal. The Gross statue was unveiled May 5, 1897. Dr. W. W. Keen, one of the eight great surgeons of the world, was the orator of the day. The statue bears the following inscription:

SAMUEL D. GROSS.

American physicians have erected
this statue to commemorate the great deeds
of a man who made such an impress
upon American surgery that it has served
to dignify American medicine.
1897.

Dr. Gross's name is one of the great names in American medicine and surgery that appear in mosaic in the ceiling of the Congressional Library at Washington.

Full of honors as of years, Dr. Gross sunk to his rest. Great as a medical teacher and investigator, greater still as a courageous and successful operator, greatest of all as a man and citizen, he left an impress upon his age and times which will probably never again be duplicated by any one man.

He is one of the few whose deeds live after them. Such as he have been characterized by a gifted poetess as being of

The immortal dead who live again
In minds made better by their presence.

Dead? No! my dear hearers. Such a name is not "born to die." Samuel David Gross, "America's foremost surgeon," *is not dead.* True enough, he has passed from the sphere of action; he has rested from his arduous labors these twenty-seven years; but "his works do follow him." He still lives in the surgical principles which he so ably advocated; and in the hearts of those of us who cherish the traditions of our time-honored profession and believe, with the people of Kentucky, that a fitting attribute of a truly great physician or surgeon is the one implied by the inscription: "The milk-white flower of a stainless life."

NOTES AND NEWS.

MEDICAL EXAMINATIONS.

TREASURY DEPARTMENT.

BUREAU OF PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE.
WASHINGTON, January 30, 1912.

A board of commissioned medical officers will be convened to meet at the Bureau of Public Health and Marine-Hospital Service, 3 B Street, S. E., Washington, D. C., Monday, April 8, 1812, at 10 o'clock a. m., for the purpose of examining candidates for admission to the grade of assistant surgeon in the Public Health and Marine-Hospital Service.

Candidates must be between 22 and 30 years of age, graduates of a reputable medical college, and must furnish testimonials from responsible persons as to their professional and moral character.

The following is the usual order of the examinations: 1, physical; 2, oral; 3, written; 4, clinical.

In addition to the physical examination, candidates are required to certify that they believe themselves free from any ailment which would disqualify them for service in any climate.

The examinations are chiefly in writing, and begin with a short autobiography of the candidate. The remainder of the written exercise consists in examination of the various branches of medicine, surgery, and hygiene.

The oral examination includes subjects of preliminary education, history, literature, and natural sciences.

The clinical examination is conducted at a hospital, and when practicable, candidates are required to perform surgical operations on a cadaver.

Successful candidates will be numbered according to their attainments on examination, and will be commissioned in the same order as vacancies occur.

Upon appointment the young officers are, as a rule, first assigned to duty at one of the large hospitals, as at Boston, New York, New Orleans, Chicago, or San Francisco.

After four years' service, assistant surgeons are entitled to examination for promotion to the grade of passed assistant surgeon.

Promotion to the grade of surgeon is made according to seniority and after due examination, as vacancies occur in that grade.

Assistant surgeons receive $1600, passed assistant surgeons $2000, and surgeons $2500, a year. When quarters are not provided, commutation at the rate of $30, $40, and $50 a month, according to grade, is allowed.

All grades above that of assistant surgeon receive longevity pay, 10 per cent in addition to the regular salary for every five years' service up to 40 per cent, after twenty years' service.

The tenure of office is permanent. Officers traveling under orders are allowed actual expenses.

For further information, or for invitation to appear before the board of examiners, address "Surgeon-General, Public Health and Marine-Hospital Service, Washington, D. C."

THE JOHNS HOPKINS HOSPITAL BULLETIN.

It is issued monthly. Volume XXIII is now in progress. The subscription price is $2.00 per year. (Foreign postage, 50 cents.) Price of cloth-bound volumes, $2.50 each.

A complete index to Vols. I-XVI of the Bulletin has been issued. Price, 50 cents, bound in cloth.

Orders should be addressed to THE JOHNS HOPKINS PRESS, BALTIMORE, MD.

NOTES ON NEW BOOKS.

Further Researches into Induced Cell-Reproduction and Cancer. Consisting of papers by H. C. Ross, M. R. C. S., J. W. Cropper, M. B., and C. H. Ross, M. R. C. S. With Illustrations. The McFadden Researches. (*London: John Murray; Philadelphia: P. Blakiston's Son & Co., 1911.*)

About a year ago, Dr. H. C. Ross wrote a book entitled "Induced Cell-Reproduction and Cancer." The sale of this work, it is said, was interfered with, more or less, by a disagreeable quarrel between the author and a committee of his scientific friends who had been selected to support and advise him in his work. These "Further Researches" are sent out with a typewritten letter by his brother, Sir Ronald Ross, which we fear will not help the sale of the work. The quarrel is not of the least importance, and we do not care to hear only one side of it, and when Sir Ronald Ross says that "Scientific men in America should know that the work is not only sound, but, in my opinion, contains a discovery of very high importance," he is casting a slur on our scientists. They do not require Sir Ronald Ross's endorsement of his brother's work upon which to found their own judgment of the work, nor are they so narrow-minded as to be led astray by a quarrel about which many of them have never heard. The less said about the quarrel the better. The original work and this supplement will be judged on their merits, and there is no fear that Dr. Ross's discoveries will be overlooked if they are important, for there is no international clique attempting to suppress his work.

A Handbook of the Diseases of the Eye and their Treatment. By Sir Henry R. Swanzy, M. D., etc., and Louis Werner, M. B., etc. Tenth Edition. With Illustrations. $4.00. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

Careful revision of this well-known work keeps it a much valued book by students and practitioners. This edition for the first time contains some colored illustrations by Dr. Werner, which will add to its popularity. As produced by the publishers it is an attractive manual in its new form and size.

Microbiology for Agricultural and Domestic Science Students. Edited by Charles E. Marshall, Professor of Bacteriology and Hygiene, Michigan Agricultural College. $2.50. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

This text-book, as stated in its title, is intended primarily for students of agriculture and domestic science, and aims "to provide the fundamental and guiding principles of the subject, and to show just how these principles fit into the subjects of a more or less strictly professional or practical nature." At least for the two special branches mentioned it has been as well done as could be expected in a course not necessarily accompanied by practical laboratory exercises. The numerous contributors have for the most part handled their subjects well, and there is neither a conspicuous lack of unity nor much unnecessary repetition. The morphology and physiology of micro-organisms receive treatment that is adequate for the purposes of the book; while the practical applications to air, water, soil, foods, and dairy products are also very good.

The division treating of microbial diseases of man and animals is hardly adequate for the needs of medical students; however, the authors have compressed most of the essential facts into a very small compass. The section on "Immunity and Susceptibility" is marred by several serious inaccuracies. For example (page 562), the writer refers the well-known complement fixation test of Bordet and Gengou to Neisser and Wechsberg, tending to confuse with it the "complement deviation" phenomenon of the latter authors. Further, in the confused description of Wright's method of determining the opsonic index (page 566), the differences between normal and diseased individuals are referred incorrectly to differences in their leucocytes, instead of to differences in their serum.

Aside from this, the book is to be commended, and should aid in extending the practical application of knowledge gained in the laboratory to the industries in question. P. W. C.

Fourth Scientific Report on the Investigations of The Imperial Cancer Research Fund. Under the direction of the Royal College of Physicians in London and the Royal College of Surgeons of England. By Dr. E. F. Bashford, General Superintendent of Research and Director of the Laboratory. Published by the Authority of the Executive Committee. 7/6. (*London: Taylor and Francis, 1911.*)

This long and admirable report is made up of three papers as follows: 1, Spontaneous Tumors in Mice, by Dr. Haaland; 2, Cancerous Ancestry and the Incidence of Cancer in Mice, by Dr. Murray; and 3, The Behavior of Tumor-Cells during Propagation, by Dr. Bashford, the Director. The first and third papers comprise most of the volume, as Dr. Murray's is but brief, though important, as it deals with the heredity of tumors in many generations of mice. This question of heredity is one of fundamental interest to all students of cancer problems, and though the data derived from animals cannot be applied directly to human beings, yet each study of this nature helps to throw some light on a very obscure point. Dr. Bashford's introduction gives to those unprepared, by lack of sufficiently detailed knowledge, to read through the report, a most illuminating résumé of the advance made in the study of many factors of this disease in the last few years. No thorough student of cancer can afford not to be at least acquainted with the findings of this Research Fund.

Oxford Medical Publications: Tuberculous Diseases of Bones and Joints. Their Pathology, Symptoms and Treatment. By Sir W. Watson Cheyne, Bart., etc. Second Edition. $5.50. (*London: Henry Frowde, and Hodder & Stoughton, 1911.*)

The true student of surgery, the specialist, will find this a most interesting work, as it represents the views of a man who has lived long enough to watch the changes that have taken place in the minds of surgeons as to the correct methods of handling these diseases, and who here expresses his own opinions after careful thought on the matter, and this author's opinions, as surgeons know, are deserving of the highest consideration. The illustrations are well chosen and sufficient in number, and the book, as a whole, is a sample of the excellent product of the Oxford University Press.

Electricity: Its Medical and Surgical Applications, Including Radiotherapy and Phototherapy. By Charles S. Potts, M. D. Illustrated. (*Philadelphia and New York: Lea & Febiger, 1911.*)

This book is divided into seven sections: 1, Electricity; 2, Electrophysiology; 3, Electrodiagnosis and Electroprognosis; 4, General Electrotherapeutics; 5, Methods of obtaining general and local effects by the indirect action of electricity; 6, Special Electrotherapeutics; and 7, The Application of the Röntgen rays in medicine, thus making a volume of nearly 500 pages of text. There is also a good index. The author's arrangement of his material is a more fortunate one than that usually employed by writers on this branch of medicine. As he says in his preface, "The custom, hitherto, has been to consider the physiological action, therapeutic uses, and methods of application of each form of current separately. In this volume, on the contrary, these subjects have been discussed collectively, according to a medical.

rather than a physical subdivision. In other words, instead of devoting one section exclusively to the constant current, another to the static current, and so on, the author has grouped these modalities according to the effects produced." This method of arrangement will certainly appeal to students, and the entire book strikes us as one that both doctors and students will find helpful and well adapted to their needs. In this work, Dr. Potts has been assisted by Drs. H. C. Richards and H. K. Pancoast, who have respectively written the chapters on Electrophysics and Röntgen Rays.

Meine Präparationsmethode des Operationsfeldes mittels Jodtinktur. Von Kgl. Rat. Dr. Antonio Grossich. 75 cents. (*Berlin und Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

Doctors, who can read German, will find this small work useful. Dr. Grossich presents a brief report on his own observations, and the possibly harmful effects of the tincture of iodine, and republishes three articles by himself on this subject, and gives an abstract of papers and personal communications by others who have tried this method of skin disinfection. The author's conclusions are: 1, that his method of preparation in the treatment of accidental injuries accomplishes a great deal, and to use a colloquialism, "cannot be beaten"; 2, that in urgent cases it is quite irreplaceable; and 3, that in aseptic operations it offers the best method. The value of the tincture of iodine as a means of disinfecting the skin cannot be seriously questioned, but we feel that Dr. Grossich goes too far in his commendation, when, to support his ideas he states that bacteria pass through invisible holes in rubber gloves during the course of an operation. This may occur, but the danger of a wound being infected in this way need not really be considered for a moment. Dr. Grossich thus tries to prove that all infections of wounds occurring after the use of iodine are due to some other cause than the inefficacy of the iodine itself. This is exaggerated, but none the less his essay is well worth study.

The Diagnosis of Nervous Diseases. By Purves Stewart, M. A., M. D., Edin., F. R. C. P., etc. Third Edition. Revised and Enlarged. (*London: Edward Arnold; New York: E. B. Treat & Co., 1911.*)

Except by the specialist, this book has not received the attention it deserves in this country. It has already been translated into French and German, and for the beginner is especially useful as "it approaches the subject of diagnosis of nervous diseases from the clinical standpoint, avoiding abstruse details of purely theoretical interest." This point of view should make it especially welcome to the student and general practitioner.

Diseases of the Digestive Canal (Œsophagus, Stomach, Intestines). By Dr. Paul Cohnheim, Berlin. From the Second German Edition. Edited and Translated by Dudley Fulton, M. D., etc. Illustrated. Second Edition. (*Philadelphia and London: J. B. Lippincott Company.*)

To physicians who do not know this book, we commend it. This group of diseases is ever a stumbling-block to the general practitioner, and from the clear exposition of them, as given by Dr. Cohnheim, he can gain much assistance. It is encouraging to note that the second German edition has been so promptly translated.

Swamp Fever in Horses. By L. Van Es, E. D. Harris, and A. F. Schalk. Bulletin 94. (*Fargo: N. D., September, 1911.*)

The North Dakota Agricultural Experiment Station has just published this report from its Department of Veterinary Science. It is an important contribution to the already large literature on a disease of horses about which little is definitely and accurately known, except that to farmers it is a question of grave importance in certain parts of the country, since the mortality among the horses affected is high. Veterinary students will be glad to have this new report, which, though it contains little that is new on the subject, deals with the disease in a satisfactory way, and helps to add a little light on some of the obscure points.

Manual of Operative Surgery. By John Fairbairn Binnie, A. M., C. M. (Aberdeen), etc. Fifth Edition. Revised and Enlarged. With 1365 Illustrations. $7.00. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

The two volumes, which made up this book when it last appeared, are now combined into one, not too large, also well printed and abundantly illustrated. In its new form it will doubtless be still more acceptable to the profession. Many of the illustrations are purely diagrammatic, and in this form are perhaps more readily understood by the student, though they do not commend themselves artistically. But this is a side-issue, and Dr. Binnie's manual is good.

Text-Book of Medical Jurisprudence and Toxicology. By John J. Reese, M. D., etc. Eighth Edition. Revised by D. J. McCarthy, M. D., etc. $3.00. (*Philadelphia: P. Blakiston's Son & Co., 1911.*)

To this well-known work the editor has merely added a few new sections on the commitment of the insane, anaphylaxis, formaldehyde and chronic bismuth poisoning. He has also revised the chapter on insanity. Thus this text-book still remains largely the work of the author, and will continue to be welcome to a large body of students.

Progressive Medicine. Vol. IV. December, 1911. Edited by Hobart Amory Hare, M. D., etc., assisted by Leighton F. Appleman, M. D., etc. (*Philadelphia and New York: Lea & Febiger, 1911.*)

This volume includes a review of recent papers in Diseases of the Digestive Tract and Allied Organs, The Liver, Pancreas and Peritoneum by Lavenson, Diseases of the Kidneys by Bradford, Genito-Urinary Diseases by Bonney, Surgery of the Extremities, Shock, Anæsthesia, Infections, Fractures and Dislocations, and Tumors by Bloodgood, and Practical Therapeutic Referendum by Landis, with an Index. The value of this work is in the presentation by specialists, who are cognizant of all the work that is being done along these lines, of the best opinion on these conditions as expressed in the current literature. Progressive Medicine is a most useful reference book for the general practitioner.

Through Rebman Company (New York) can be secured, free of charge, a well arranged catalogue of the post-graduate medical work at the University of Vienna, prepared by the publishers, Urban & Schwarzenberg (Berlin & Vienna). This gives a list of the teachers, of the courses and lectures and places where they are given, and is printed in English, French and German, side by side, so as to be most convenient and useful for any student or doctor thinking of going to Vienna to pursue his medical studies.

P. Blakiston's Son & Co., of Philadelphia, have published their annual Physician's Visiting List for 1912. It is a vest-pocket memorandum book with its serviceable tables of dosage, poisons and their antidotes, etc., which many a practitioner will find useful.

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NARCOSIS.*

By Dr. Max Verworn,
Professor of Physiology, University of Bonn, Germany.

Mr. President, Ladies and Gentlemen:

Two main reasons induced me to select the subject of narcosis for my lecture before your society. On the one hand, I am following herein the suggestion of your honored president; on the other hand, the problem of narcosis has a personal attraction for me, since I and my colleagues at Göttingen, as well as in Bonn, have devoted a great deal of attention to its investigation. Furthermore, I believe that this theme, the subject of narcosis, possesses an especial interest for medical men, not only from the theoretical but also from the practical side. From the theoretical side, because the processes of narcosis introduce us into the most profound secrets of the mechanism of living matter; from the practical side, because it is incumbent upon the physician to know the actual nature of the condition, which he so often induces in man. Practical and theoretical interest have here, once more, the same object. Such union of practical and theoretical interests makes our medical work so fruitful and lends it a special charm among the biological sciences. This is especially manifest in the study of the peculiar phenomena of narcosis, and is also the reason why the subject of narcosis has been so extensively investigated, especially in the last decades.

The knowledge of the use of narcotic substances, especially those from the vegetable kingdom, is ancient. It extends back to prehistoric times, as we may deduce by analogy with primitive races living to-day. Man has been, from the first, a student of nature. He was forced to adapt himself, at every step, to his environment. This he could do only by very close observation of nature, for there was danger lurking for him wherever, in his wanderings, he was confronted with new conditions. Thus, in his quest for food he had to learn to recognize the peculiar poisonous effects of plants. All primitive races are familiar with them and employ them for various purposes. The use of narcotizing substances, especially for purposes of enchantment, was well-known in the Homeric age. Circe mixed narcotic juices with the food of the companions of Odysseus, making them forget their homes; and Hermes knew already an antidote, which he gave to Odysseus as a protection: μῶλυ δὲ μὶν καλέουσι θεοί. In Homer we also find, for the first time, although not in connection with poisonous action, the word from which the modern term "narcosis" is derived. The verb ναρκάω, "I am paralyzed," appears in Homer as ἅπαξ εἰρημένον when he describes how Hector struck Teukros on the shoulder with a sharp stone, so that his hand, paralyzed, let fall the bow (Iliad VIII, 328). This venerable word serves us to-day to distinguish a special group of paralyses, or depressions, which are induced by chemical substances.

* Lecture delivered before the Harvey Society in New York, October 28, 1911, and before the Johns Hopkins Hospital Medical Society, October 31, 1911. The secretary of the Harvey Society has kindly granted us permission to publish this paper in advance of its appearance in the proceedings of the Harvey Society.

The scientific study of narcosis begins, however, only with the time when narcotics came into general use in medical practice for the relief of pain, especially since, in Boston, in 1846, the chemist Jackson and the dentist Morton introduced ether into surgical practice. Soon after this momentous event experiments began for the purpose of explaining the striking action of anesthetics. Among the numerous explanatory efforts, however, there are only two series of attempts which deserve scientific consideration.

In one series, it has been tried to establish a relation between the depressing action of narcotics and their solubility in certain constituents of the organism. As early as 1847, Bibra and Harless used the fact that cerebral fats are readily soluble in such narcotics as ether and chloroform, as a basis for a hypothesis of the mode of action of narcotics. They assumed that the narcotics act as anesthetics by extracting the brain-fats. Hermann indicated later a similar conception, and recently Reicher has shown that in deep and long-continued narcosis the fat-content of the blood rises indeed quite markedly. While already in these assumptions the relations of solubility between fats and narcotics stand in the foreground, Richet has later on called attention to a second relation in regard to solubility. He noticed that many narcotics were distinguished by a very low degree of solubility in water, and believed that, on the basis of his observations, he could make the general statement that a substance acts the more strongly as a narcotic, the less it is soluble in water. The relations between the solubility of narcotics in fats and water and their depressing action, which in the before-mentioned observations and hypotheses were expressed so incompletely and obscurely, were first made clear and formulated according to definite laws by Overton and by Meyer, independently of one another. Hans Meyer and Overton were able to show that the intensity of the narcotic action of any substance is dependent on the proportion in which it is distributed between water and fat when it is shaken with a mixture of fat and water. The coefficient of distribution, that is, the proportion of solubility of the substance between water and fat, is the greater, the stronger its narcotic action. That is to say, a substance acts the more strongly as a narcotic, the more soluble it is in fats and lipoids and the less soluble it is in water. Meyer and Overton have confirmed this law on a very large number of narcotics. This interesting fact contains apparently a very important requirement for the production of narcotics, although it does not present a "theory of narcotics," as has often been incorrectly stated. It shows us one factor that must be realized if the narcotic is to reach its field of action, but it tells us nothing concerning the mechanism of the narcotizing action itself.

The second series of explanatory attempts ascribes the depressing action in narcosis to a change in the state of aggregation of certain components of the protoplasm under the influence of the narcotic. Claude Bernard, who noticed the rigidity of muscles which is produced by the influence of chloroform vapor or heat, was the first one to express the view that narcosis consists in a "semi-coagulation" of the protoplasm. Binz came to the same conclusion from a microscopic study of ganglion cells and unicellular organisms. He found that the protoplasm of the cells became opaque, granular and dark under the influence of the narcotic, as is the case in coagulation, and he sees therefore, in narcosis, a depression by coagulation. As a matter of fact, it is easy to observe such changes in unicellular organisms under the influence of large doses of narcotics, but recovery from such a state is no longer possible. In recent times, Höber has expressed similar opinions. Höber makes the hypothesis that the process of excitation is associated with a loosening of the protoplasmic colloids, which consist of lipoids and proteids. In connection with this assumption, Höber offers the further hypothesis that narcotics inhibit this loosening of the colloids, especially in the superficial protoplasmic layers of the cell, so that in consequence the irritability is reduced or abolished.

Thus, we see that widely different hypotheses concerning the nature of narcosis have been expressed, without any of them having as yet achieved general acceptance.

Before we attempt to form a conception of the mechanism of narcosis, it appears to me indispensable that we clearly understand what should be required of any theory of narcosis. Narcosis is a state of living matter, in which, under the influence of certain chemical substances, the physiological processes of the cell are altered in a special way. A scientific study of this state can only consist in seeking to determine, as far as possible, the nature of these changes. The more deeply we analyze them, the clearer becomes the theory of narcosis. In order, however, to comprehend the changes in the physiological processes in living matter, it is requisite that we should first know the normal physiological processes themselves, in all their details. In spite of many important and fundamental researches, we are to-day still far from such knowledge. From this it is evident that we cannot yet speak of a "final" theory of narcosis. But where in our knowledge do we arrive at final results? Wherever we may look, whatever we may achieve, we are always and again confronted with new problems. Is there, anyway, a finality anywhere? Whoever, impatiently rushing forward, looks for a final word in knowledge will, like Goethe's Faust, only experience grievous disappointment:

> "Entbehren sollst Du, sollst entbehren!
> Das ist der ewige Gesang,
> Der jedem an die Ohren klingt,
> Den unser ganzes Leben lang
> Uns heiser jede Stunde singt."

On the other hand, whoever is conscious that all things stand in endless coherence will desist from seeking an imaginary goal, and instead will enjoy the inexpressible charm which lies in the unlimited possibilities of finding again and again new links of this coherence The possibilities of knowledge are endless, because the world is endless. This is true in large as well as in small things, and is true also of our problem. To the extent to which we succeed in discovering new facts which characterize the state of narcosis, to that extent the theory of narcosis develops of itself.

Well, then, what do we know of the changes which living

matter undergoes during narcosis? Narcosis is a state of depression. Let us understand what this means. All states of depression in living systems are characterized by the fact that all or single partial processes of the normal metabolism undergo a retardation of their course, which may amount to complete standstill. This shows itself in the following symptom-complex. The specific manifestations of life of that system are depressed or extinguished. The irritability to external stimuli is lowered, so that stimuli which are effective in the normal state, show no apparent result. At the same time the power of conductivity, that is, the transmission of the excitation from the point of stimulation to some distant place, is correspondingly restricted, for irritability and conductivity run always and everywhere along parallel lines. This symptom-complex occurs in the most diverse living systems and under the influence of manifold agencies. We see it as a result of low temperatures in "frigor depression," or as a result of high temperatures in "heat depression"; we meet it after extreme functional activity as fatigue; after withdrawal of oxygen, as suffocation; under the influence of chemical substances, as toxic depression; after too low osmotic pressures of the surrounding medium, as "water rigor"; from stoppage of the blood-supply to the tissue cells, as asphyxial depression; and under many other conditions.

The question now arises, whether the mechanism of the depressing process is the same under all these widely diverse circumstances. In its generality, we can at once answer this question in the negative. The mechanism of depression in water rigor and in acid-intoxication, for instance, is entirely different. Nevertheless, comparative studies of the mechanism of depression under the influence of different factors have shown me that a particular tendency exists toward one etiologic type of depression. In the complex realm of metabolism in all aërobic forms of cell, one part of the many anabolic and catabolic processes is especially sensitive to external influences, and that is the oxygen metabolism. Here is, in a certain sense, the *locus minoris resistentiæ* of the living matter of all aërobic organisms. In fatigue, it is the relative deficiency of oxygen which produces the depression. The increased demand for oxygen, brought about by the increased functional activity, can no longer be satisfied by the amount of oxygen present. The same is true of heat depression. The supply of oxygen cannot keep pace with the accelerated catabolism of the living tissue, induced by the temperature. In the asphyxial depression of the tissue cells which occurs as a result of any stoppage of the blood-supply, it is not the withdrawal of the organic nutritive materials in the blood, but only the lack of oxygen, which produces the depression. In prussic-acid poisoning, again, it is the suppression of the oxygen metabolism in the tissue cells which produces death. Thus we see that oxygenation is the factor, in the metabolism of aërobic cells, which most easily fails under diverse external influences and so forms the starting-point for the development of depression.

The most simple paradigm of this entire group of depressions is therefore suffocation of living cells or tissues in indifferent media free of oxygen. Fortunately we know to a certain extent the working of the mechanism of suffocation.

In normal metabolism during rest the supply of oxygen is always sufficient for the needs of the cells. Molecular oxygen is absorbed by them from the surrounding medium. A certain reserve supply of molecular oxygen, although comparatively small, is always present in the cells themselves, at least in cold-blooded animals not kept at too high a temperature. Many facts force us to this opinion, especially the continuance of normal production of energy and of irritability for a longer or shorter time, under complete exclusion of oxygen supply. The oxygen taken up from the medium is activated by special oxygen-carriers and distributed to the oxidizable substances. We know of the existence of such oxygen-carriers in the most diverse animal and vegetable cells, and we are accustomed to group them together under the collective name of "oxydases," although their chemical constitution is still completely unknown. The oxygen-carriers bring activated oxygen, in the manner of inorganic catalysators, to the oxidizable substances, which by the oxidation are split into carbon dioxide and water. One point here remains still undecided, and that is, whether the oxidation attacks the organic fuel directly, such as, for instance, the carbohydrates, which have been synthetically built up by anabolic processes, or whether only the fragments are oxidized to carbon dioxide and water, while the splitting itself is accomplished by enzymatic processes. It is possible that in different forms of living substances the catabolism takes a different course. At any rate, the principal source of energy in all aërobic organisms is to be found in the oxidative splitting-up processes, and not in the non-oxidative part of the catabolism. These oxidative splitting-up processes represent the principal source of energy-production. That is an important fact. It has a special bearing upon the degree of irritability of living matter, for irritability is measured by the amount of energy-production which results from a stimulus.

What changes does this phase of metabolism undergo, when the external supply of oxygen is withdrawn from a living system? No more molecular oxygen enters the living matter from the outside. The molecular oxygen, which at the moment of exclusion of oxygen is still present in the living tissue, will, according to its amount, be used up sooner or later. In the same proportion the extent of the oxidative breakdown will decrease. The catabolism will occur more and more in a non-oxidative manner. As soon as all the oxygen is used up, the destructive process will be entirely non-oxidative. This gradual transition from oxidative to exclusively non-oxidative decomposition corresponds in a characteristic way to the development of the depression. The intensity of the spontaneous vital activities diminishes gradually after the interruption of the external supply of oxygen. Very gradually the irritability for external stimuli decreases. Very gradually also the extension of the excitation from the point of stimulation to adjacent parts becomes restricted. Finally no spontaneous manifestations of life are visible; finally no visible effect

is to be obtained from the strongest external stimuli. These are the general consequences which result from an interruption of the oxygen supply and which we observe everywhere in whatever way and at whatever point the oxygen metabolism is disturbed.

I have dwelt in some detail on the relations of the metabolism of oxygen and its disturbances, because our investigations carried out in the laboratories at Göttingen and Bonn have shown that in narcosis, also, there is a similar interference with the oxidation process. The fact that the oxygen metabolism suffers readily under diverse external influences, suggested the question whether also, under the influence of narcotics, disturbances of the oxidative processes take place. I had previously studied, by means of an artificial circulation, the rôle of oxygen metabolism in fatigue of the spinal cord of the frog, made especially sensitive by mild strychnin poisoning. It seemed to me, from my experience, that this would be a favorable object for the experimental determination of the question whether the oxidative processes are interfered with during narcosis. This question could be particularly well studied on the fatigued spinal cord, because it was found that the fatigue can be completely removed again only by the supply of oxygen. If the spinal cord is fatigued and oxygen is not supplied, as can easily be done with an artificial circulation, and if now the completely fatigued and oxygen-greedy spinal cord is narcotized, it can be determined whether, with a free supply of oxygen, the spinal cord can take it up, and thus recover during narcosis. If the fatigued cord is irrigated during narcosis with arterial ox blood or with an oxygen containing saline solution, and later, while the narcosis still continues, the blood is removed again by oxygen-free salt solution, and if then the narcosis is stopped, it must become manifest whether the centers of the cord have taken up the abundantly supplied oxygen during narcosis, and recovered. Winterstein has performed this experiment at Göttingen, using various narcotics, such as ether, alcohol, chloroform and carbon dioxide. All the experiments agreed in showing that not the least trace of recuperation occurred; while, after the end of the experiment, the cord was completely restored in a few minutes by perfusion with oxygenated ox blood without narcosis. Herewith the first proof was given that, during narcosis, living tissues are unable to utilize the oxygen offered to them.

Nerves offered a second favorable object for testing our question. We had succeeded, after many vain attempts, in perfecting a method by which it was possible to show that nerves died of suffocation when cut off from all possible supply of oxygen. This fact, established by H. von Baeyer, placed us in a position to make on the nerve, which proved to be an exceedingly favorable object, experiments on the question of oxygen metabolism during narcosis analogous to those made on the cord. The sciatic nerve of the frog was asphyxiated, and thus made oxygen-greedy. When its conductivity was lost and its irritability reduced to a very low level, it was narcotized with ether. Then, during narcosis, oxygen was supplied to it for a long time. After the oxygen had been finally removed by pure nitrogen, the narcosis was stopped. In these experiments, which were first made by myself, afterwards by Fröhlich, and later on by Heaton, there was never any trace of recovery. When the nitrogen was replaced by air, the nerve recovered in one minute and showed normal irritability and restoration of conductivity.

Finally, in a series of experiments which have not yet been published, Ischikawa proved that amœbæ, also, which have been asphyxiated in a gas-chamber in pure nitrogen and have become motionless, did not take up oxygen which was supplied to them during narcosis, while after stopping the narcosis and replacing nitrogen by air they rapidly resumed their amœboid motion.

These experiments show unequivocally *that living tissues, even when their demand for oxygen has been raised to an extreme degree by fatigue or asphyxia, cannot, during narcosis, make use of oxygen, even when offered to them abundantly.*

This conclusion caused us to advance one step further. If living tissue, during narcosis, cannot use the oxygen which is supplied to it, this inability might be produced in several ways. Either narcosis depresses the entire phase of catabolism, with all its partial processes, perhaps by paralyzing the first step, or it hinders especially only the oxidation processes. In the former case, we should expect that a narcosis of a certain depth, in which the destructive processes were completely abrogated, could continue for an indefinite time. In the second alternative, that is, if only the oxidation is prevented, destruction must proceed in non-oxidative form, just as in the absence of external oxygen supply, and the living tissue under narcosis must eventually die of asphyxia, even though sufficient oxygen is constantly at its disposal. We can decide between these two possibilities. On the one hand, experience shows that no narcosis, whatever its depth, can continue indefinitely without the tissue losing its viability. On the other hand, we can demonstrate experimentally that during narcosis catabolism proceeds in non-oxidative manner and that asphyxia gradually supervenes. Here again the nerve proved to be a favorable object for experiment. Heaton has used the two sciatic nerves of the same frog for the following parallel experiment: One nerve was drawn through a gas-chamber which contained pure nitrogen; the other was narcotized in a similar gas-chamber filled with air. The experiments began simultaneously in the two nerves. In the asphyxiated nerve the irritability sank very gradually lower and lower. When it had fallen to a certain level, the conductivity for an excitation coming from the part of the nerve outside of the gas-chamber vanished also. The time at which this degree of depression is reached depends on the length of the asphyxiated portion of the nerve, on the condition of the frog, and on the temperature. At room temperature it requires, on the average, from two to three hours. At the time that the conductivity of the asphyxiated nerve was abolished, the air surrounding the narcotized nerve was replaced by pure nitrogen, and the narcosis interrupted, so that the nerve, after the narcosis was

stopped, had no more oxygen at its disposal. If the whole destructive phase of metabolism had been brought to a stop, the nerve should, after stopping the narcosis, be in about the same condition as before it. This was, however, not the case. All the experiments, rather, agreed that during narcosis this nerve was also asphyxiated like the nerve in pure nitrogen, in spite of the fact that the former always had air at its disposal. Its irritability had been greatly reduced and its conductivity was abolished. That it was actually asphyxiated was shown by the control experiment, in which both nerves recovered completely as soon as air was conducted over them. The irritability increased rapidly and the conductivity returned.

Ischikawa has recently performed similar experiments on amœbæ. Amœbæ gradually lose, in nitrogen, their amœboid motions. They regain them only when oxygen is supplied. If amœbæ are narcotized with ether, they are also asphyxiated; for after the narcosis, in the absence of oxygen, they do not regain their amœboid motions. These only return after oxygen is supplied.

It is thus evident that living tissue is asphyxiated during narcosis; that is, that the destructive phase of metabolism proceeds in a non-oxidative manner.

We can add yet another fact. Even during narcosis *the destructive processes can be increased, that is, accelerated, by exciting stimuli.* Heaton has narcotized the two sciatic nerves of a frog in a double chamber under absolutely identical conditions. While one of them remained at rest, the other was continually stimulated by a faradic current applied to the end beyond the chamber. After discontinuing the narcosis in pure nitrogen it was always found that the irritability of the stimulated nerve had fallen to a lower level than that of the other. Placed in air, both recovered to an equal degree. The results of this experiment entirely agree with the phenomena of fatigue, which were found by Thörner in his researches on the fatigue of nerves in nitrogen. On the basis of all these experiments, we may make the following statement: *Living tissue becomes asphyxiated during narcosis. The catabolic phase of metabolism continues in the form of a non-oxidative destruction, just as in asphyxia, and can also, as in asphyxia, be accelerated by exciting stimuli. Recovery from this asphyxia is, as in every asphyxia, only to be attained by supplying oxygen.*

Under these circumstances the idea naturally presents itself, that the entire symptom-complex of narcosis is only a manifestation of asphyxia, which the narcotic induces by inhibition of the oxidative processes. Before we accept this idea, however, we must assure ourselves that there is no fact which stands in the way of its acceptance. It goes without saying, that if asphyxia occurs in narcosis, the general picture of asphyxia must be present. This is actually the case. The cessation of spontaneous evidences of life, the reduction of irritability, the decreased power of conductivity—all the typical symptoms are identical in narcosis and in asphyxia in an oxygen-free medium. In only one point is there a noteworthy difference. *That is in the time relations of the depression-symptoms.* In narcosis of nerves, for instance, irritability sinks *in a few minutes* to a point which in pure nitrogen is only reached in *two or three hours.* The question therefore arises, whether we have not here a fact which must inevitably eliminate the idea that narcosis is nothing more than asphyxia. A more careful consideration shows, however, that this is not the case. The experiments which have already been described contain the explanation of this difference in the rapidity of onset of the depression.

The fact that living cells, during narcosis, can make no use of molecular oxygen, even when it is freely offered to them, shows that the narcotic renders the living tissue incapable of undergoing oxidations. It cannot, therefore, utilize for its oxidation processes the oxygen present in itself. The conditions during asphyxia in an oxygen-free medium are, however, quite different, as for instance in asphyxia of nerves in nitrogen. Here the power to carry on oxidations is not interfered with in the least. As long as any trace of molecular oxygen is present, it can be used for oxidation. Now it is of course impossible that, at the moment that the air in a gas-chamber is replaced by nitrogen, every trace of oxygen should disappear from the nerve in the chamber. The nerve, therefore, with its small oxygen requirement, can, even in pure nitrogen, carry on its oxidation processes in a more or less decreasing degree, according to the temperature and to the amount of oxygen contained in the nerve itself. Accordingly, the irritability decreases only gradually, and in proportion to the extent of the decrease of the oxidative processes. *In the depression of nerves in an oxygen-free medium we deal with a slow, while in narcosis we deal with an acute, asphyxia.* That is the factor which produces the difference in time. We have also, therefore, the power of eliminating this difference completely. We may do this, in one way, by those measures which hasten asphyxia in an oxygen-free medium. Such a measure is the increase of the demand for oxygen by raising the temperature. In this case heat depression occurs. Of heat depression we know that it is an asphyxia which results from a relative lack of oxygen, because the supply of oxygen cannot keep pace with the markedly increased demands of the living tissue, just as in fatigue. As H. von Baeyer has shown, complete loss of irritability in nerves may be attained by keeping them for 20 minutes in a gas-chamber at a temperature of 42° to 47° C. The lost irritability cannot be restored by reduction of temperature alone; while, after supplying the nerve with fresh air, recovery results in a few minutes. At higher temperatures asphyxia occurs still more rapidly. In the ganglion cells of the cerebral cortex of mammals, asphyxia results in a few seconds when the air supply is cut off. On the other hand, the narcosis of the nerves can be greatly delayed if the narcotic is administered only in small amounts. In short, *the more rapid or slower onset of depression is solely dependent on the rapidity with which the oxidation processes are abolished.* In narcosis this occurs very rapidly, because the narcotic renders the cells incapable of carrying on oxida-

tions; in asphyxia in oxygen-free media, it occurs only very slowly, because the living tissue retains its power to carry on oxidation and continues to do so until the last trace of oxygen present in the tissues is used up. The difference in the time of development of the depression in the two cases is solely dependent on the different way in which the oxidation processes are brought to a standstill. The symptom-complex of narcosis, therefore, not only is comprehensible, but on the basis of the ascertaind facts it is a requirement.

It seems to me that, after these considerations, it is no longer possible to doubt, not only that narcosis is accompanied by asphyxia, but that the acute asphyxia is the deciding factor which produces the depression. This does not exclude the possibility that the narcotic may also produce other changes in the living matter, for instance changes in the state of aggregation of certain substances. Whatever other changes may occur, *the factor which produces the characteristic symptom-complex of narcosis is under all circumstances the suppression of the power to carry on oxidations.*

The conclusions which may be drawn directly from the facts bring us this far; but the problems are by no means finished. At this juncture the new question arises: In what way does the narcotic, by entering the cell, inhibit the power of the latter to carry on oxidations? Here the facts leave us still in the dark. If we wish to answer this question, it can only be done in the form of a hypothesis. I wish to emphasize this point particularly. But "*no true scientist fails to realize that the essential factor of progress lies in a hypothesis which agrees with the facts.*" These words of one of the greatest physiologists, who was also my predecessor in Bonn, shall serve as my excuse if I attempt now, with the assistance of a working hypothesis, to go a step further in the direction indicated.

When we recall the fate of molecular oxygen in the normal metabolism of the cells, from the moment at which it enters the living substance to the moment at which it decomposes the oxidizable materials into carbon dioxide and water, we find that the narcotic, which overflows the cell, could establish its inhibitory action upon the oxidation at various stages of this process.

In the first place we might conceive *that the narcotic, when it has penetrated into the living substance, prevents in some way the entrance of molecular oxygen from the surrounding medium into the cell.* This assumption, however, may be dismissed at once. If the depression of narcosis were produced by the fact that oxygen could not penetrate into the cells, then we could expect a course of depression with exactly the same time relations as in complete withdrawal of external oxygen; the cell would be in exactly the same position as it is, for instance, in pure nitrogen. The difference in the time relations between the two cases, for instance in the nerves, shows us, however, that this is not the case.

Next we must consider the possibility *that narcotics appropriate the oxygen which enters the cells, and use it for their own oxidation.* The narcotics are, it is true, generally looked upon as chemically indifferent substances, but Bürker has recently published experiments which show that, under certain conditions, narcotics may be oxidized, at least by nascent oxygen. Bürker performed the following interesting experiment. He placed two identical voltameters in the same electric circuit. One of them was filled with acidulated water; the other had in addition a small percentage of ether. Then he decomposed the fluids electrolytically by means of a galvanic current. In the voltameter which contained no ether, the gas collected at the two poles in the usual relation, the volume of hydrogen at the cathode being to the volume of oxygen at the anode as 2 to 1. The relationship was, however, entirely different in the voltameter which contained ether. Here only a very small amount of oxygen collected at the anode; while the analysis of the gas from the anode showed that carbon dioxide, acetaldehyde and acetic acid had also been formed, as oxidation products of ether. Based on this result, Bürker put forward the hypothesis that narcotics had the same effect in living substance as in the voltameter, and that the depression of the oxidation process in narcosis depends on the fact that the narcotic itself appropriates the oxygen. As, in living tissue, oxygen is activated by oxygen-carriers, the possibility of oxidation of ether even in the cells is not, indeed, excluded. But under the conditions which obtain in living tissue, it is doubtful whether it really occurs to such a degree as to reduce the oxidation of respiratory materials to a noticeable extent. For many of the narcotics, oxidation in the cells is very unlikely, and in the case of carbon dioxide it is absolutely excluded.

A third possibility of the interference with oxidation is, *that the narcotic in some way blocks the molecules of oxidizable material, perhaps by a loose chemical fixation, and thus renders them inaccessible to oxidation,* and the oxidation will thus cease. However, this view also has very little likelihood. According to this view, we would have to presuppose that the narcotics, which in themselves present substances with very heterogeneous chemical properties, were also able to block very diversified substances; for in non-oxidative catabolism, such as occurs in narcosis, manifold products arise with very different chemical properties. We would have to assume that all these different substances can be prevented from oxidation by all the different narcotics. We cannot readily have recourse to such an assumption.

Finally, there remains one more possibility to be considered. It might be assumed *that the narcotic renders the oxygen-carriers incapable of activating the oxygen, so that the oxidizable materials could no longer be oxidized and decomposition would proceed only in non-oxidative form.* This view seems to me the most probable, as we have inorganic analogies for it. The colloidal solutions of metals, for instance platinum solution, can, as Bredig has shown, be prevented from acting as oxygen-carriers by diverse chemical substances, such as corrosive sublimate, hydrogen sulphide, hydrocyanic acid, etc. "Paralyses," or depressions, are produced in this way, which correspond to a great extent with the depressions of living

cells. If I therefore form the hypothesis that narcotics, in an analogous way, render the oxygen-carriers in living tissues incapable of carrying oxygen, all the facts of narcosis find a simple mechanical explanation.

But still more; the possibility is also given, here, to combine the relation between the solubility in lipoids and narcotic action, discovered by Overton and Meyer, with the facts already given concerning the influence of narcotics on oxidation processes. The fact that the lipoid solubility of a substance primarily determines the degree of its narcotic action, shows us that the mechanism which lies at the base of the symptom-complex of narcosis must be associated in some way with lipoids. We have seen that this mechanism consists in an inhibition of oxidations, and it is highly probable that this comes about through a paralysis of the oxygen-carriers. It is quite natural to assume that the oxygen-carriers, whose chemical nature is still entirely unknown to us, stand in some close relation to the lipoids, that they are perhaps themselves of lipoid nature, or that they are attached as specific atom groups to lipoid molecules. By this assumption the relations discovered by Hans Meyer and Overton and the facts shown by us, that narcosis depends on acute asphyxia, would be combined in a natural manner. Both facts would mutually complete each other, and the result would be a further elucidation of the mechanism of narcosis.

However, I wish to emphasize, again, that the conception regarding the nature of inhibition of oxygen metabolism in narcosis is of a purely hypothetical character. It is only an established fact *that narcotics induce an acute asphyxia of the cells. Herein is the essence of narcosis.*

If we are satisfied, for the present, with this knowledge and leave the question of the particular mechanism of the asphyxia to one side, the mere fact that narcotics inhibit oxidation processes will in itself guard us from many false conceptions in regard to narcosis. The knowledge of this fact has some significance also for the practical use of narcosis.

Let us ask, first, what we narcotize when we induce narcosis in man by inhalation of ether or chloroform. All tissues of the body are not affected equally by any means. Even if it is assumed that the blood carries the narcotic to all the tissues in nearly the same concentration, the different tissues are influenced to a very different extent by the narcotic. When the ganglion cells are already completely depressed, the nerve-fibers and muscles still show no sign of narcosis. The ganglion cells of the brain, and especially those of the cerebral cortex, are most readily affected in their specific functions by narcotics. Thus, if we induce so-called "general" anesthesia by ether or chloroform narcosis for any operative purpose, we deal in reality only with narcosis of the cerebral cortex. In this lies the great value of narcosis; for we desire in narcosis to eliminate conscious sensation, and the acts of consciousness are, as is well-known, due to excitation of the ganglion cells of the cerebral cortex. The ganglion cells of the cerebral cortex, with their functions intact, are the most valuable asset that man possesses. Therefore it is particularly important to us that nothing shall happen which might injure them permanently, and we must therefore know the possible dangers of narcosis, in order to avoid them.

The fact that the ganglion cells of the cerebral cortex lose their specific functional activity, under the influence of narcotics, sooner than any other body cells, must, on the basis of our new data in regard to the relationship of narcosis and asphyxia, naturally give rise to the idea that they are more sensitive to asphyxia than any other body cells. That is actually the fact to a striking extent. Mosso has demonstrated this in a classic way on man, in whom alone direct studies of the conditions of the processes of consciousness can be made. In his experiments on Bertino, he found that a few seconds interruption of the supply of oxygen sufficed to produce loss of consciousness. Bertino had a large defect in his skull over the frontal lobe, and the cerebral pulsation could be graphically recorded there. The frontal lobe receives its blood supply from branches of the carotid arteries. When Mosso compressed these arteries in the neck, so that the cerebral pulsation ceased, Bertino lost consciousness in five seconds without having had any premonitory disagreeable sensations. After releasing the pressure upon the carotid arteries, consciousness returned at once. This experiment shows how dependent the cells of the cerebral cortex are on their supply of oxygen, and in how short a time unconsciousness occurs after complete interruption of this supply. Here we have an example of a depression rapidly following the withdrawal of oxygen. The associative workings of our ideas and sensations, thoughts and feelings can proceed in an undisturbed manner only when there is complete integrity of the specific irritability of all the ganglion cells concerned. The slightest loss of irritability interrupts the orderly play of excitations and inhibits the activity of consciousness.

From this peculiarity of the cortical cells is the important requirement derived, long known empirically, that in man we should employ a light degree of narcosis, just sufficient to paralyze consciousness. Under such circumstances the depression of the oxidative processes is undoubtedly of very limited extent, and there is no demonstrable danger of permanent injury to the normal brain. When we employ a deeper narcosis, the danger of rapid and complete asphyxia of the ganglion cells increases with the depth of the narcosis. At any rate it ought to be always present in our mind that the deeper the narcosis the more it inhibits oxidation processes, and that the ganglion cells of the cerebral cortex are exceedingly sensitive to lack of oxygen. Here we deal with the most tender and perishable cells of our body.

In this connection I wish, before concluding, to point out an error that has been handed down from olden times, and even at present has not been corrected everywhere. It is the identification of narcosis with sleep.

The origin of this confusion is evident. It is based on the entirely superficial analogy that both states are characterized by loss of consciousness. But not every loss of consciousness is sleep. This confusion, which may have been justified in

earlier times, when both conditions were known only by their external symptoms, is to-day, when we have penetrated somewhat more deeply into the inner processes of the cells of the cerebral cortex, a grave mistake. Closer consideration will show this plainly.

What occurs in the neurons of the cerebral cortex during an act of consciousness? I am far from intending to give here a detailed analysis of these processes. I wish to emphasize only a single general fact. Let us conceive a condition of the cerebral cortex in which the neurons are in metabolic equilibrium; that is, in which the two phases of metabolism, the anabolic and catabolic phases, balance each other. We should have then a state of complete rest, in which no act of consciousness takes place. An act of consciousness ensues only when the metabolic equilibrium in a chain of associated neurons is disturbed by an exciting stimulus which causes a sudden increase of the catabolic phase. Every act of consciousness is the expression of a catabolic disturbance in the cortical neurons. This is not merely an assumption; it is shown, among other things, by the fact that even the simplest conscious process requires the associated co-operation of several ganglion-cell stations, and that on the other hand the nerve fibers which provide for this associated co-operation conduct no other impulses except catabolic excitation processes. On this general basis, for all processes of consciousness there are two possible origins of unconsciousness. Loss of consciousness will occur either because the ganglion cells are depressed, so that the external stimuli produce no excitation, or because exciting stimuli are absent. As we have seen, the first condition prevails in narcosis; the irritability is so much depressed that stimulation is ineffective. In sleep, the second alternative is predominant; the first plays at most the rôle of a predisposing part for the induction of sleep. We sleep, and determine the moment of going to sleep, by limiting as far as possible the sensory stimuli, especially the optical. This state of the utmost exclusion of external stimuli lasts throughout the entire period of sleep. This is supported to a certain extent by fatigue, that is, the decrease of irritability, which the ganglion cells have sustained by the constant action of sensory stimuli while awake during the day. A comparison of the processes which occur in the ganglion cells of the cerebral cortex during sleep and during narcosis will show us plainly how diametrically opposed these are.

During sleep, restitution occurs. The irritability, which becomes reduced in the course of the day as a result of the fatiguing action of sensory stimuli, gradually rises again. The fatigue of the ganglion cells, which, as we know, depends only on a relative lack of oxygen, becomes completely dispelled. The supply of oxygen, which during constant activity was not quite sufficient to keep irritability at its maximum, is, after the cessation of functional demands, fully sufficient to banish the fatigue. In short, during sleep, restoration occurs principally by the action of oxygen. In the morning the ganglion cells are refreshed and possess their full capacity for work.

How different is narcosis! In narcosis there is, on the contrary, as we have seen, a depression of the oxidation processes. The experiments showed that even with a free supply of oxygen a fatigued ganglion cell did not recover at all during narcosis. There occurs, rather, a gradual asphyxia, and, although this process is only developed to a small extent in light narcosis, still it presents just the reverse of that which sleep brings to the ganglion cells. In the one case, recovery from fatigue by oxidation; in the other, prevention of restitution by inhibition of the oxidation process. There can be no confusion between sleep and narcosis.

If we use narcotics to induce sleep, we must always bear in mind that no true sleep occurs as long as the narcosis of the cortex lasts. We can speak of "hypnotics," or "remedies for sleep" (*Schlafmittel*), only in the sense that, when there is constant excitation of the ganglion cells, they reduce irritability and induce a greater degree of depression, so that true sleep may take place as the narcosis passes off. In that sense a hypnotic may prove beneficial in the hands of the physician, and when used sparingly. The physician must, however, never forget that not the entire period of unconsciousness which follows the use of the hypnotic is true sleep, but that at first it is, rather, a depression, the injurious effects of which will manifest themselves when the hypnotic is used for a longer period.

Ladies and Gentlemen: I am at the end of my lecture. The facts which I have stated take us, I believe, a step forward in the analysis of narcosis. They show us the general nature of the process, which is merely one of the great group of depressive actions which depend on a disturbance of the oxygen metabolism. They open however, at the same time, a number of new questions. The previously mentioned hypothesis concerning the method by which narcotics inhibit the process of oxidation, shows us the direction in which these questions lie. It may serve us as a guide for the present. The further analysis of the process will principally have to determine the nature of the transmission of oxygen and in what way this is affected by the narcotic. The experiences of modern physical chemistry will be of great help to us in the study of this question. I may, however, take this opportunity of warning against a misuse of physical chemistry in the explanation of biological facts; and this the more, since this misuse, which has grown with the development of that science, is already beginning to arouse in the minds of many biologists a strong distrust of the value of physical chemistry in the analysis of biological processes. It is frequently believed that a biological process is explained when the terminology and certain catchwords, I might almost say the scientific "jargon," of physical chemistry have been applied to biological relations. There has been recently, for example, a great misuse of the word "colloidal process." There is positively nothing gained by it when a biological phenomenon (for instance, excitation or depression) is designated as colloidal process. This is neither correct nor incorrect; it says nothing. That the living tissues contain various colloid substances, and that these colloids undergo alterations in the course of the vital processes, has long been known. We wish, however, to know what it is that happens to the colloids, which of their properties are altered

and how these changes are incorporated into the machinery of the cell. For this purpose patient and careful analysis is required, and not the introduction of mere catch-words. The methods and results of physical chemistry give us very valuable material for such analysis; but it would be very one-sided to consider the methods of physical chemistry only. The methods and results of chemistry, physics and microscopical research must be employed, as well as those of physical chemistry. In short, every method must be employed which will bring us a step further. That alone can be the general principle of all physiological research, and this principle will also lead up to new knowledge in the investigation of narcosis.

A BRIEF NOTICE OF FELIX PLATTER, WITH EXTRACTS FROM HIS MS. MEMOIRS PRESERVED AT THE LIBRARY OF BÂLE.[1]

By Charles Greene Cumston, M. D., Boston, Mass.

In selecting the subject of Felix Platter for an address, I have done so because the man has been little known, although undoubtedly his reputation as a physician, as well as his writings, are certainly familiar to those of our profession who are more or less occupied or intimately concerned with the history of medicine.

Then again, I shall refer to his memoirs, the manuscript copy of which is preserved in the University of Bâle and I believe in giving extracts therefrom, which relate more particularly to medicine, a certain amount of interesting matter heretofore unknown to many medical historians, will be brought to light. Among the numerous manuscripts from the hand of Felix Platter deposited in the Public Library at Bâle, are to be found something over two hundred detached leaves which, so to speak, together form a diary, although they contain much information quite foreign to the person of the writer. From these MS. leaves I have selected only those portions pertaining more particularly to medicine and I must confess that they give the best description of student life and medical customs of those early days that I have ever come across. The time and place of study were those of the great philosopher and erudite Rabelais. What more need be said?

The subject of this address was born in 1536 of a distinguished father, Thomas Platter. Of his early life little will be said excepting that when Platter was very young he evinced a pronounced taste in the first place for poetry and music, then afterwards for show and dress which considerably occupied his thoughts. Nevertheless, the paternal advice always stood fast by him: the Dukes of Wurtemberg and the sister of Henry IV, Catherine, Duchess de Bar, were desirous of attaching him to their courts but in spite of their brilliant and reiterated offers he refused to leave Bâle. Besides Catherine de Bourbon and the Princes of the house of Wurtemburg, to whom he gave his professional care for more than forty years, Felix Platter comprised among his clients the Margraves of Baden and Brandebourg, the Dukes of Lorraine and Saxony. The most distinguished physicians of the time, as well as scientific bodies, had recourse to his knowledge. By a fortune always rare in a small country, his talents were promptly recognized and accepted by his compatriots. Received Doctor of Medicine at the age of twenty-one years, he was immediately elected member of the "consilium medicum." He had not, however, attained the required age and much comment was again made when the chair of the practice of medicine was confided to him in 1571, at the death of Jean Huber to whom he also succeeded by unanimous decision of the Council in the functions of city physician, or as it was termed *archiater,* which position invested with him the direction of the hospitals as well as the care of watching over the public health. He retained this position to the end of his life, in other words during a period of forty-three years. At the time of the plague of 1563-'64, his devotion obtained for him a universal gratitude. While several of his colleagues were careful of their person and another fled to Frankfort, Felix Platter supervised everything. The epidemic carried off his servant and a young man who was living with him, it seized upon his father, his mother, and all their household, but he fulfilled his duty with courage, braving the contagion at each step. Upon four other occasions, in 1576, 1582, 1593, and 1609, he was again face to face with the same scourge. Curiously enough, he and his wife were never affected; only upon one occasion, having committed the imprudence to hold the hand of a dying patient, a sore developed on his hand but fortunately the infection remained localized.

As a professor he was in no way inferior to the practitioner. A rich experience, a clear, methodical and penetrating mind, combined with an elegance of elocution readily explains why Platter became an eminent teacher and that his disciples loved him for his affable and gentle character, likewise his untiring zeal and enthusiasm. Haller (Biblioth. anat., 1, 255) calls him the star of the University of Bâle; this epithet is quite justified if one will reflect upon the impulse given to the Faculty of Medicine by Platter, seconded by Theodore Zwinger and Gaspard Bauhin.

Upon his return to his native town, Platter found only one or two medical students, but in the year 1575 there were already fifteen matriculated. From 1532 to 1560 only nine degrees of Doctor of Medicine had been given; during the twenty-five following years the number of degrees reached one hundred and fourteen while it attained four hundred and fifty-four in the period comprised between the year 1586 to

[1] Paper read at a meeting of the Book and Journal Club of the Medical and Chirurgical Faculty of Maryland, Baltimore, February 6, 1912.

1610. German, Dutch, Hungarian, Italian, French and English students flocked to Bâle and were proud of the honor of receiving their degree of M. D. from the University.

Two innovations contributed to this prosperity, namely, dissection and the creation of a chair of botany and anatomy. This initiative belongs to Platter. As a student at the Faculty of Montpellier, which at this time was distinguished from the majority of other schools in that each year the professors publicly dissected two or three cadavers, he had followed these operations with the greatest interest, overcoming the repugnance that his naturally timid and impressionable nature caused. He had hardly returned to Bâle when he performed an autopsy before a large audience, an event which had not taken place in that town since the days of Andreas Vesalius. However, the installation of Gaspard Bauhin as professor of anatomy and botany, the establishment of an amphitheatre and of a medicinal garden, only date from the year 1589.

Felix Platter only wrote late in life and he was nearly fifty when, in 1583, he gave the printer his work entitled: *De corporis humani structura et usu.* Then twenty years passed by before he published his *Praxeos medicæ,* the first volume of which appeared in 1602, the third and last in 1608. Many editions of this manual of pathology and therapeutics succeeded each other at short intervals up to the year of 1736, a success all the more remarkable because it corresponds to that period during which medicine was undergoing a complete transformation. And lastly, when nearly an octogenarian and having behind him fifty-seven years of practice, Platter published his *Observationum in hominis affectibus* which contained the fruit of his long experience.

If these works have not always been appreciated at their just value, it is usually because one has lost sight of the object for which they were written, viz., the instruction of students. Plater has particularly been reproached in that his first work, that on anatomy, contains only plates reproduced after those of Vesalius. On this point our author explains himself with perfect frankness, for he distinctly states: "As up to the present time the plates of Vesalius are the best that have ever been offered, and as it would be almost impossible to surpass them, I would have willingly added them to this volume introducing a few slight changes (because the opportunity presented itself for buying them), if I had not been prevented from this intention by the necessity of adopting under the circumstances a large size volume which would be very inconvenient for students. That is why I have had engraved on copper, reducing them in size and slightly changing them, the plates of Vesalius that I have completed by adding a few others." Several of the figures are new or present more details than those of Vesalius and, consequently, there can be no question of plagiarism on the part of Platter.

Scientific knowledge without literary culture produces a dryness of the mind and the development of pedantism, whose inseparable companion is a poverty of ideas. On the other hand much is due to letters in many a discovery made in various domains which are foreign to them. Thomas Platter impressed his son Felix with the importance of the dead languages and it was not likely, in point of fact, that these would be unknown to him at a time when, thanks to the vogue of Galen and Hippocrates, the chair of Greek was almost always filled by a physician. From this classical education, Felix Platter derived a promptitude of intelligence and a gift of analysis, two qualities which not a little contributed to his renown. In reality, his successes as a practitioner are in a less degree due to his complicated prescriptions, composed of thirty or forty ingredients, than to his great skill in diagnosis. His *Praxeos medicæ* is recommendable in the first place by a rational classification of diseases, which are studied according to their nature and not merely in relation to their seat. His observations on insanity give evidence of a remarkable insight to diseases of the mind and he protests against the heartless and barbarous treatment to which the insane were in those days subjected; he endeavored to obtain a cure by adopting a method which takes into consideration the moral phenomena, and, consequently, it is not too much to say that Platter was a fore-runner of the immortal Pinel.

In endeavoring to discover morbid causes by post-mortem examinations, Platter certainly inaugurated pathological anatomy. And, lastly, he pointed out the utility of exact statistics, when at the time of the epidemics of plague he drew up the census of the city, street by street, indicating for each house the number of its inhabitants, their names and their civil condition, the number of cases occurring in each epidemic, likewise the deaths, and all this work was undertaken when his mind was full of other medical preoccupations but which, nevertheless, remains as a most precious historic document.

This originality of view is quite in accord with the freshness of mind that the taste for poetry kept up in Felix Platter to the very last of his life. As an old man he was pleased to compose bits of verse both serious and light. When near his end he wrote his epitaph, a rough translation of which I will here give, although much of its beauty is naturally lost. "Upon this earth my vocation was to study the works of God and to apply myself, from my early youth, to turn them to His glory as well as to the well being of my fellow creatures. Now my soul enjoys celestial felicity: it contemplates the magnificences of the Lord, until that time when He shall resuscitate it with my body on the day of Judgment."

Plater was always a lover of music while plants and animals also occupied his leisure moments. His magnificent garden containing rare plants and vegetables which he himself cultivated, was the admiration of all. Rich was his collection of objects of art and natural history, which unfortunately was dispersed during the eighteenth century. The memoirs of de Thou, the historian, contain the following relative to Platter:

Il visita Félix Plater, docteur en médicine, logé dans une grande et agréable maison, et qui le reçut fort civilement. Plater lui fit voir dans son écurie une espèce d'âne sauvage, de la grandeur des mulets de Toscane ou d'Auvergne, le corps court et de longues jambes, la corne du pied fendue comme celle d'une biche, quoique plus grosse, le poil hérissé et d'une couleur jaunâtre et brune. Il lui montra encore un rat de montagne de la grandeur d'un chat, qu'ils appellent une marmotte: ce petit animal étoit enfermé dans

une cassette, et comme it avoit passé l'hiver sans manger, il étoit tout engourdi. Plater avoit aussi l'étui des fossiles de Conrad Gesner venue de Zurich, tel qu'il est décrit et dessiné dans un de ses livres. Cet étui renfermoit bien des raretés différentes, entre autres quantité d'insects particuliers, qui semblent autant de jeux de la nature. De Thou les examina à loisir et avec une grande curiosité, aidé de d'Amerbach, qui s'y connoissoit fort bien.

In the following year, viz., 1580, it was the turn of our dear Montaigne. In his "Voyage en Italie," speaking of Bâle the following paragraph will be found:

Nous y vîmes de singulier la maison d'un medicin nommé Félix Platerus, la plus peinte et enrichie de mignardises à la françoise qu'il est possible de voir; laquelle ledit médicin a bâtie fort grande, ample et somptueuse. Entre autre choses, il dresse un livre des simples qui est deja fort avancé; et au lieu que les autres font peindre les herbes selon leurs couleurs, lui a trouvé l'art de les coller toutes naturelles si proprement sur le papier, que les moindres feuilles et fibres y apparoissent comme elles sont, et il feuillette son livre, sans que rien en échappe; et montra des simples qui y étoient collés y avoit plus de vingt ans. Nous vîmes aussi et chez lui et en école publique des anatomies entières d'hommes morts, qui se tiennent. . . . Nous y vîmes [at Bâle] *force gens de savoir, comme Grineus, et celui qui a fait le Theatrum, et ledit médicin (Platerus), et Francois Hottoman. Ces deux derniers vinrent souper avec messieurs, lendemain qu'ils furent arrivés.*

Felix Platter died of dropsy on July 28, 1614, after a fortnight of great suffering. Only twice during his long life was he seriously ill. His wife had died eleven months before; their married life had been fifty-six years, and the only unhappiness casting a shadow over their union was the absence of children. They both left a large amount of money to be used for giving gratuitous medical treatment to the poor. Platter was buried in the cloister of the cathedral in Bâle and his stone, placed beside that of his father, bears the following inscription:

C. S.
Archiatro Basil. Dignissimo,
Urbis imo orbis Aescvlapio,
Acad. Professori Celeberrimo
Annos XLIII, Continvos,
Qui Rector Magnif. Sextum Fuit,
Quique Uno in Coniugio exoptatiss.
Cum Magdal. Ieckelman Matron. Lectiss.
Ante Annum Pie Defuncta,
Maritus vixit Annos LVI.
Doctor Vero Annos LVII.
Felici Platero Thomae F.
Naturae, Artisque Operum
Indagatori Solertissimo,
Conquisitori copiosissimo,
Medicorum suae Aetat. Principi
Nomine et Omine Felici,
Viro Probo, Probis Omnib. Probata,
In Egenos Liberali,
In Omnes Officioso,
Phthisi Sen. in Sed. Beat.
Sublato:
At Salutaribus Inventis,
Ingeniique Monumentis,
Aeternum Victuro,
Thomas Platerus D. Prof. Anat. Bot.
Fratri, Potius Patri Desideratiss.
M. H. P.
Vixit Annos. LXXVII M. IX.
Obitt Anno Sal. M. D. C. XIV. IVL. XXIIX.

I will now make extracts from Platter's diary, only selecting those portions which bear directly on his student life and medical subjects. I would point out that Catalan was an apothecary at Montpellier with whom he lived during three years that he studied in this city and that the Dr. Saporta to whom he refers was a famous professor and practitioner whose family originally came from Spain and whose ancestors were well known physicians in the epoch in which they lived. Rabelais refers to Saporta as a fellow student. Platter arrived in Montpellier some time in the latter part of October, 1553, and returned to Bâle on February 24, 1557. After giving a thrilling account of his journey to Montpellier and of his arrival in that city he says:

I at once began to follow the lectures. As is the custom each student chooses a preceptor, to whom he may refer for advice, and so I selected Dr. Saporta. I gave myself up seriously to the study of medicine; I listened to two or three lectures in the morning and as many in the afternoon. The letters and pressing exhortations of my father greatly stimulated me; I worked with great zeal, which greatly pleased my old host Catalan. He always spoke Latin to me according to his way, that is to say very badly, and when I replied in a rather more correct manner, he was very greatly astonished.

The running of my master's house was extremely economical, following the Spanish custom. It should be known that the Marans[2] do not use any of the food which the Jews abstain from. On the days we eat meat we had for dinner a mutton soup (but rarely beef) with small turnips and cabbage; it was good but the bouillon was not abundant. Each one had his plate and ate with the fingers. Afterwards came the roast. The wine was not wanting; it is a dark red and is mixed with much water. You have the servant pour for you into your glass the quantity of water you desire, then the wine is added; the servant throws away the wine that you leave because it cannot be kept for more than a year as it rapidly transforms into vinegar.

My master changed his pharmacy. I followed him to his new spacious and pleasing house. A room was given me for my use. Later on, with plates, I arranged the upper room for a study; I ornamented it with pictures, my host had a guilded arm chair put in for me (because he always took good care of me), so that when people came into the room each one was in ecstacy. The hall ended upon a beautiful terrace from which the entire city could be seen; the view extended as far as the sea, whose grumblings I could hear from time to time. It was here that I sat while studying; I cultivated the Indian fig tree which was developed from a slip sent to him from Spain. Often I sat at the window and played the lute; the people who lived opposite, a Monsieur Saint-George, and particularly his sister, Miss Martha, listened to me with pleasure.

With the advent of the new year a large number of diversions commenced, particularly gallant serenades at night in front of the houses. The same individual played upon the cymbals, drum and fife; the hautbois was also known, even quite generally played upon while the violincello and guitar were just becoming fashionable. The notable bourgeois gave balls to which the young ladies were taken; after supper dancing in the torch light was resorted to. These assemblies continued until daylight. The balls only ceased at the last day of the carnival.

We celebrated Epiphany at the Collegium among us Germans; the old beadle prepared the delicacies and the cake; Andreas de Croatie got the bean. Two days later we again celebrated

[2] The Marans were the descendants of the Moors that Ferdinand, the Catholic, expelled from Spain. Many came to Montpellier.

Epiphany at the house of Rondeletius.[3] As the Germans were reconducting by torch light some of their comrades, they were accosted by the captain of the watch who started to disarm them. From this resulted a great tumult in front of my host's pharmacy. Stephanus Contzenus obstinately refused to give up his dagger; Master Catalan having come out, begged him to give the arm to him; this was done and order was again restored. On the very next day the Germans made a complaint before the bailiff for violation of their franchises. The captain was blamed and we were assured that such an abuse would not occur again.

On the Sunday of the Quinquagesime (our *Herrenfastnacht* (Shrove-Sunday)), there was dancing throughout the entire city; everywhere accords of music could be heard and everywhere there were masquerades of a thousand different kinds. These festivities continued on Monday and the following day, which is called Mardi gras. On this day the young people form a procession: around the neck they carried a bag filled with oranges (their very low price in this country, a dozen only costing about two cents) and a basket on the arm in guise of a shield. When they reached the Place Nôtre-Dame, they began throwing the oranges at each other's heads and soon the pavement was covered with the débris. On the same Tuesday, the doctors of law went through the different quarters of the city disguised.

With Ash Wednesday Lent commences, during which it is forbidden, under the penalty of life, to eat either meat or eggs. It is quite true that we Germans transgressed this order by stealth. It was at this time that I learned how to spread butter on a sheet of paper, break the eggs on this and cook them over the heated coals; prudence demanded that no utensils should be employed. During Lent I cooked eggs over the candle, they being spread on buttered paper, and then I threw the shells into my study; later on a servant discovered this mass of shells; she told her mistress who displayed a very marked displeasure, but did not push the inquest any further. It is the custom to break the pots which have been used for cooking meat and to buy new ones in which to cook the fish.

A gentleman, one of our neighbors, invited me on a certain day to a nocturnal concert in honor of a young lady; this is what is called an aubade. At midnight we came before the house. We commenced by beating a drum in order to wake up the inhabitants of the quarter; then trumpets were heard, afterwards the hautbois, after the hautbois the fifes, after the fifes the violincellos and lastly three lutes, the entire performance lasted certainly three quarters of an hour. We were then conducted to a pastry cook where we were largely treated; we drank muscat and hyppocras and the night was passed in festivities.

My father sent me two beautiful skins dyed green; I had a garment made with them embroidered with green silk in which I strutted about and excited the envy of the gentlemen at the assemblies of dance. I arranged with a lame boot maker, whom we called Vulcan, that he was to bring me a new pair of shoes each Sunday; for the entire year this only cost me three francs, that is to say ten of our batzen.[4]

Although there are many physicians who do not take the trouble to become learned in their art, I always felt myself forced to learn everything that a doctor should know. At each instant I repeatedly heard how many physicians there were at Bâle; consequently, at my return there it would be necessary for me to make my way and even to rise above my colleagues. On the other hand, I was fully aware that my father was laden with debts, that his position only gave him a small compensation, that his boarders were his principal financial resource, and that, consequently, it would hardly be possible for him to help me. He himself wrote me to in no way count on his fortune, that he was not a rich man, but merely a schoolmaster, a poor peasant; that I was to make my calculation as if I had no fortune to be left me, or at the most a very small amount. How could one then foresee that he would again marry at a very advanced age and that he would bring forth such a numerous posterity?

All these circumstances caused me not only to study and follow the lectures with assiduity, but also to attentively watch in the pharmacy the manner in which medicines are prepared. My master had a large practice: consequently I derived much profit from the time spent in his laboratory. And still more, I collected a large number of plants that I delicately fixed on paper. But above all things I was desirous of knowing anatomy. I, consequently, never failed to be present when a cadaver was secretly opened. At the beginning, this operation was extremely repulsive to me; nevertheless, with some Welch students, I ran more than one risk in order to obtain subjects. Frequent dissections took place at the house of Gallotus, who had married a lady of Montpellier and enjoyed a certain fortune. He convened us to go armed outside of the city to dig up secretly, in the cemeteries adjacent to the cloisters, the bodies which had been buried on the same day; we carried them to his house, where we proceeded to the autopsy. Certain individuals were present at burials and then they would lead us to the grave.

My first expedition of this kind dates from December 11, 1554. The night was already dark when Gallotus lead us outside the city to the monastery of the Augustins. We there found an adventurous monk who had disguised himself and gave us his help. We entered furtively into the cloister, where we remained drinking until midnight. Then, well armed, and observing the greatest silence we went to the cemetery of the convent of St. Denis. Myconius had his sword drawn while the Welchmen had their daggers unsheathed. We dug up the corpse with only our hands, because the earth had not had time to become compact. When once the cadaver was brought to light a rope was passed round it and, pulling with all our might, we brought it up to the surface; after having enveloped it in our cloaks, we carried it on two rods up to the entrance of the city. It might have been about three o'clock in the morning. We placed our load in a corner and then knocked at the gate. An old porter presented himself in his shirt and opened; we begged him to give us a drink, pretexting that we were dying of thirst. While he went to get the wine three of us brought the cadaver in and carried it to Gallotus' house which was not far away. The porter suspected nothing. As to the monks of St. Denis, they found themselves obliged to guard the cemetery and from their cloister they fired with their arbalest[5] on the students who presented themselves.

The theatrum often served for dissections, which were then presided over by a professor; a barber manipulated the scalpel. Beside the students the audience contained a large number of noblemen and citizens, ladies as well, even when one dissected a male; many monks also came there. I exercised myself a little in distilling. I took note of a large number of receipts that the doctors gave me or which I borrowed from works of Falco; the latter were inherited by my host from Falco himself; he kept them under key in a room into which I introduced myself by a ladder not without danger. I was also indebted to the knowledge of excellent remedies either to Kirchmannus who had them from the physician Faber, of Cologne, or to students who brought them back from Italy and with whom I discussed science. I put in writing the *loci communes in tota medicina;* I reduced into tables the most important books of Galen; I heard Rondeletius express his strange opinions of which I took careful note. Once we passed

[3] Rondelet was a very celebrated physician and Chancellor of the University of Montpellier. The character of Dr. Rondebilis in Rabelais' writings is simply a caricature of the eminent professor.

[4] A batz was a piece of money used at Bâle, in value being about six cents

[5] A cross-bow.

an entire night copying a book: *De componendis medicamentis*, that Rondeletius loaned us; we were careful not to omit a receipt for causing hair to grow, because still being without a beard, we thought that a mustache would give us a more respectable appearance: how many times in the evening have we besmirched our lips, which resulted in soiling the pillows; we also scraped under the nose with a razor, but all these fine means were not at all efficacious.

At this time, Humelius informed me that his pharmacy was not at all profitable, that few remedies were prescribed, that the people of Bâle were not at all anxious in having skilful physicians, that the prescriptions were rather more German than Latin. The majority of physicians purged with senna, licorice and other absurd receipts. Dr. Isaac conducted himself as a quack of the lowest order. In brief, it was better to be a beggar than an apothecary at Bâle. All that the physicians knew how to do was to purge; as to potent medicines, like those prescribed at Montpellier, there was no question of them. Humulius, consequently counted on me to reform this condition of affairs. His letters stimulated me; I could foresee the possibility of rising above my colleagues and of introducing several novelties such as the enema, topics and a large number of excellent specifics. By the grace of God this did happen.

My father warned me not to permit myself to care for my German comrades, on account of the punishment that one ran the risk of receiving at Montpellier if one practiced the art of healing without having a diploma: such offenders are placed astride the back of an ass, facing the animal's rear, whose tail they hold in the place of reins; then they are led through the streets in the midst of the laughter of the populace, finally they are conducted out of the town and during the entire course the children amuse themselves by covering them with mud.

On March third, 1555, Guilelmus Eduardus was received doctor of medicine. The promotion, presided over by Saporta, was celebrated in the church with great solemnity and to the sound of organs. The recipient rendered grace in five or six languages, among which German, although he did not know the others. He was given a very pleasant promenade through the city; a silk plume decorated his square bonnet; the hautbois played; branches of cinnamon and little figures of sugar were carried in the processsion. There was a magnificent collation: more than a quintal of dragées were thrown about; the hyppocras was excellent; afterwards came the dancing.

On May 28th, 1556, I was received bachelor of medicine; Dr. Saporta performed the promotion at the *collegium regium*. The doctors of medicine of the University argued against me; the actus lasted from six to nine o'clock in the morning. After which I put on a red robe and rendered thanks by a carmen in which the Germans were not forgotten. In the beginning, I had recited by heart a long oration. Finally I paid eleven francs and three sous, for which I received a diploma bearing a seal. The Germans presented their congratulations to me; in order to show my appreciation, I offered them a banquet.

About this time a tumult occurred. The students reproached the professors for not giving their lectures. They assembled and armed they marched around the college and those who were there listening to a lecture were invited to come out and join the rest. It was thus that Hoechstetter came to ask me to join while I was at Saporta's lecture; I did not feel like giving offence to this professor, but Hoechstetter would not listen to me and I was finally obliged to go towards the house of parliament with an enormous crowd of students of all nationalities. There our procurator complained in our name of the neglect of the doctors and demanded the re-establishment of the ancient custom by which two procuratores, elected by the students, were invested in the right to retain the stipendia belonging to the professors who failed to give their lectures. The doctors replied by the mouth of a procurator; nevertheless, our request was granted and the tumult subsided. My father wrote me how happy he was to think that we Germans were not disturbed on account of religion. As it had come to his ears that I was quite as good a dancer as a lute player, he ended his letter by begging me not to become in love with a Welch girl, because he was doing everything in his power to give me a most agreeable wife as soon as I should return to my native country. He revealed to me the negotiations he had commenced with Master Franz Jeckelmann. The latter did not say no, but he wished to await my return before deciding anything. My father highly praised the young lady, her virtues, her judgment and her docility. He had for a long time suspected, and my comrade Hummel had recently confirmed him in this idea, that the young person was pleasing to me; for this reason he made me these overtures sooner than it was perhaps proper, but so that I would be all the more hasty in completing my *cursus studiorum* and return to Bâle. He advised me to follow my studies with ardor and not to neglect surgery.

"Great," said he, "is our penury in surgeons; the majority are children who are lacking in knowledge and experience. A difficult case comes up (?) They tremble like wet hens, scratching their heads in secret but before people *promittunt salutem*. What is the result? The patients remain deformed, when they do not die. It is necessary under such conditions that the physician should know how to advise and give assistance or even take the knife in hand; the profit is quite worth the trouble. My son, the desire of thy father is to give in thee to the country an honest man, distinguished and useful. At Bâle the number of physicians is frightful and if one is not capable of surpassing his confrères, one is sure of remaining for all his life a kind of beggar unless he should become an aulicus and engage himself in a foreign country. Now, above all things, I want to guard thee with us. He who has the greatest talent is the one who will espouse the wife of his choice."

I wrote home, admitting that the young lady had been dear to me for a long time; I only asked for the time to be received doctor and to return to my country, because the hope of obtaining her hand removed from my thoughts any idea of settling elsewhere than in Bâle. I added that the will of her father was not sufficient, that it was necessary to obtain her consent, and I begged my father to find out her sentiments when the occasion should present itself. One night I dreamed that I had a pain in my hand and that I went to consult the barber Jeckelmann, when his daughter applied something to the suffering member and I felt myself healed. Upon awaking I took this dream to mean a promise of our union.

Some time after this several of my compatriots and school friends arrived at Montpellier. They carried long Swiss swords, their costumes being completely German. One would have taken them for German foot soldiers, their manners were gross. By them I received a large number of letters. My father informed me how he had acquitted himself of my errand, viz. to ascertain what I desired to know: an enterprise not easy of undertaking, because the young lady only went out to go to church, without taking into consideration the fact that rumor was abroad that there was an understanding between herself and me. Finally my father was able to speak to her alone: he told her that I desired to know if she took pleasure in my person and if, God helping, she would accept me upon my return when I should ask for her hand. Blushing, she had replied that what pleased her father would also please her; she had always heard me spoken of favorably and had always held me in high esteem. For that matter, for a long time I had been most agreeable to her and this fact she had let be seen by the god-mother of her father, the old Schultheiss Fren, because she had admitted to the latter never to have felt for anyone as much inclination as she had for me. Consequently, she would wait for me. She had the intention of

going on a certain Sunday on a promenade with the family in the neighborhood of Gumdeldingen, and my father proposed to offer them a collation. It is readily comprehensible that this letter filled me with joy and courage. I sent Master Jeckelmann and to his daughter two beautiful embroidered cushions, some excellent Cyprus wine and two large branches of coral.

On August 25th, 1556, I received letters from Bâle, among which five sheets of paper folded like a book in octavo and completely covered with my father's writing. He showed that he was satisfied in knowing that I was working steadily to arrive *ad gradum;* he hoped that the next year would see me back in my country because Master Jeckelmann commenced to be impatient: numerous pretenders to his daughter's hand, several of whom of very excellent family, did not allow him any rest. My father also perceived that, on account of the good will which she had towards me, my future wife would salute my return with pleasure and that she sighed for that time to come. "And those who have been refused repeat: We want to see what a fine doctor he will make, he who supplants us in the estimation of Barber Franz! Have I need of telling you more along these lines? The entire city is filled with the news that Master Jeckelmann has assuredly promised thee his daughter and that from this time on it is useless for anyone to present himself. If thou couldst only hear all the talk which is made it would excite thee to confound some day those who reproached thee with thine happiness. But if thou preoccupy thyself above all to render glory to God, to fill me with satisfaction and be useful to the country, there is more than is necessary to encourage thee in thine work." My father also said that I would receive great praise by taking my degree of doctor at Bâle rather than elsewhere: the magistrates and the bourgeoisie would look upon this with a better eye than if I imitated those who take their promotion in a foreign country and who are reputed too incapable of taking the degree at our university; because one knows the saying: *Accipimus pecuniam et mittimus stultos in Germaniam.*

In November 1556 I resolved to return to the paternal roof in the following spring, by the way of Toulouse, Paris and France. My host bought me a horse and supplied me with the necessaries for the journey; my father had some money waiting for me at Paris. I was to have a companion, Theodorus Birckmannus, of Cologne, an erudite young man who not only knew how to play string instruments, but also the fife, so that is was easy for us to amuse ourselves upon the slightest occasion during our journey. A neighbor sold the horse and I disposed of my good lute not without regret. The twenty-fourth of February we treated our comrades at the inn and bade them good-bye. I called upon my professors and other acquaintances, also upon a few young ladies. The twenty-seventh of February I bade good-bye to Monsieur Catalanus who cried, likewise his wife and his servants. Brickmann arrived in front of the pharmacy with the Germans who wished to conduct us on our start. I straddled my horse and, God aiding, but with a very heavy heart in leaving this good city where I had so long time dwelt, I started off escorted by quite a numerous suite on horseback. Then I was seized by fright in thinking of the dangers which might assail me during the long trip and at the thought that I would never again see Montpellier, my heart became tender, my eyes moistened with tears.

As has already been pointed out, Platter arrived in Bâle early in the year 1557 and I will now quote his description of the taking of the degree of doctor of medicine in his native city, which is all the more curious and interesting, because it is a description given by the candidate himself.

The time had come to take my doctorate. Wishing to furnish a preliminary proof of my knowledge before making an official demand, I begged of the Faculty of Medicine the permission to profess at the *collegium* during the canicule, which was at once accorded me. Immediately I prepared myself. I sold my horse for one half of his original cost; my father took the sum, so that I was very short of money. Great was my ardor in working. On July 21, after having, on the preceding Sunday, put up notices on the doors of the church that I was to give a course of lectures, I gave my first lecture at the *collegium* in the *aula medicorum.* I commenced by a long peroration. Then I undertook the explanation of the *liber Galeni de causis morborum.* At the beginning nearly all of the doctors and the majority of the professors figured in the audience, but at the end there were only two Dutchmen remaining. On going out from the lecture they accompanied me to my home, climbed the mulberry trees in my father's garden and regaled themselves with their fruit. I showed them some curiosities in order to encourage them to follow my lectures with assiduity.

On August 14, I went to Dr. Oswaldus Berus,[6] Dean of the Faculty, and in an oration I postulated the *gradus medicus.* Thereupon I was assigned for the next day, Sunday afternoon, at the house of this same Dr. Oswaldus behind the cathedral where the three professors composing the *collegium medicum* met together. After having heard my harangue requesting the degree, they finally came to the censure: I proved that I had studied for so many years, then I showed my diplomas of Master and Bachelor of Medicine obtained at Montpellier. The professors appeared satisfied; but when they asked my age and I replied that I would be twenty-one years October next, the Decanus entered into a discourse in order to declare that the candidate should be at least twenty-four years of age. They consequently sent me away. I entered my home extremely put out, persuaded that my youth was to be an obstacle to my promotion. The same evening I told my troubles to my future father-in-law; he became angry: "If they make any difficulties," cried he, "I will give you my horse and you may go and obtain your diploma at Montpellier." However, I tormented myself gratuitously because the professors had not taken seriously their objection and they regretted that I had left so quickly.

On the next day, August 16, the beadle came to notify me for the *tentamen,* which took place in the house of Dr. Oswaldus before the three same personages. They interrogated me lengthily, particularly on medical questions; I replied to them with alacrity, it was not as difficult as I had imagined. The examination lasted three complete hours, after which they gave me the two *puncta* to explain the next day, viz., an aphorism of Hippocrates: *mutationes temporum pariunt morbos,* and the *definitio medicinæ Gal. in arte parva: medicina est scientia salubrium,* etc. At the end of this séance, Margaret, Dr. Oswald's daughter, served us with cake and wine; then the professors were extremely gay with me; for that matter, it was I who paid.

I passed the examination the next day, August 17, in the same place. I was compelled to expatiate *memoriter,* for the lapse of about an hour, on the *themata* which had been given me, just exactly as if I were professing. Then the three doctors took up the speech in order to refute my argument and this lasted full three hours; Dr. Oswald especially, who considered himself a great philosopher, worried me quite lengthily. Finally, I was allowed to retire; then I was called back and was informed according to custom, that in a short time I should be obliged to uphold a public debate. Following this we partook of a collation for which I paid, along with a little gift to Dr. Oswald's daughter.

I prepared myself for the debate. I received two short *themata*

[6] Oswald Ber, received doctor of medicine at Bâle in 1512, appointed professor in 1513, remained dean at the Faculty of Medicine from 1520 to the time of his death in 1567. He was rector in 1529 when the University was closed and it was he himself who re-opened it as rector in 1532.

from the Dean; they were not too much to my liking, and if the candidate had had, as he has today, the right of choosing, I should have preferred a more ample subject. I had these *themata* printed with a few commentaries, and on Sunday, August 29, they were posted at the four parish churches; the beadle carried copies to all the doctors and professors at the same time notifying them of the debate. This was fixed for the following Thursday. Now, on Monday, I was taken with fever, accompanied by a catarrh: it was a disease called the croup which was prevalent at that time. I was, consequently, very uncomfortable. The epidemic spread far and near. Later on I learned that it had appeared at Montpellier, at which place it was called the whooping cough. Nevertheless, on Thursday, September 2, I presented myself for upholding the debate which took place in the *aula medicorum;* it commenced at seven o'clock in the morning and lasted untill noon. Nearly all the academicians were present because there had not been a debate for a long time. The doctors of medicine alone spoke (there were hardly more than one or two students at this time; the professors Huberus and Isaacus gave them the lectures), but the masters of philosophy also mixed in with the discussion. By the aid of God, I got out of it not without honor. The seance once ended, I was obliged to regale an entire table full of guests at The Crown. After the repast, I hied myself to the usual meeting place to tell my joy to Madeleine.

On September 6, the members of the Faculty requested me to come to them in order to announce that I was admitted to the doctorate and to congratulate me. As soon as they had notified me at my house of the day and time of the promotion, I made the necessary arrangements. I had been assigned two promotores: Dr. Isaac, gave me the *themata* of my discourse, and Dr. Oswald Ber was appointed to give me the insignia. I had the notification printed, and the following Saturday, accompanied by Dr. Isaac and the beadle, I went to invite *ad actum* the burgomasters, scholars, academicians and a large number of my good friends, among whom my future father-in-law.

On Monday, September 26, I was conducted to the house of Dean Ber. Here we drank malmsey, then the procession proceeded to the *collegium.* I wore a garment of black woolen, embroidered on all the seams with a band of velvet the breadth of a hand; I wore red tights and a pourpoint of silk of the same color. In front of Dr. Huber's house, Dr. Oswald suddenly remembered that I should also dissert without preparation on a subject given at the time, and as he had forgotten to bring a book with him, he had one taken from the study of Dr. Huber.[7] We arrived at the *aula medicorum.* It was draped with rich tapestries and filled with people because for a long time back there had been no doctor's promotion. I took my place in the lower cathedra, Dr. Isaac in the upper one. The trumpets sounded, and Dr. Isaac having pronounced a discourse, proposed the *themata* to me. Immediately I recited my oration by heart, although it was long; then Dr. Isaac passed me over to the Dean and left the chair. Dr. Oswald received me with a short allocution, and preceded by the beadle carrying the sceptre, we mounted into the upper chair. There, with the customary solemnity, the Dean placed a velvet cap on my head and then upon it a beautiful crown; in short, he accomplished all the customary ceremonies, without forgetting the ring which he placed on my finger. After having proclaimed me doctor, he ordered me to give a sample of my knowledge by at once treating the first subject offered. He looked through his book and designated a place; I read as if the text of my thesis was found printed there, and then I began to dissert. After a moment, the Dean closed the book, saying that that was sufficient; then he gave me the privilege of speaking so that I might offer up my thanks, which I did in a long harangue that I had learned by heart. This was the last act of the ceremony; it had lasted more than four hours. The four trumpets again sounded and we left in procession to go to The Crown, where the banquet was prepared. The rector, Wolfgang Wissenburg, walked by my side; then came the venerable Dr. Amberbach and other academicians in quite a large number: in front of me the beadle and the four musicians marched, playing all the way. At the repast, there were seven tables; we were very well treated and it only cost me four batzen a head. The dinner ended at three o'clock because the banquets were not so prolonged then as they are at present. According to custom, the guests preceded by the sceptre were bade farewell to by Dr. Isaac. He then led me to his residence where we had a collation. After which I was conducted to the paternal roof.

Immediately after his promotion to the grade of doctor, Platter was married, the details of which happy occasion he enters into at length in his journal. What he says gives a very excellent insight into the customs of those days, but as I wish to hold to the medical portions of his journal more particularly, I shall immediately proceed to translate what he says of physicians and the practice of medicine at Bâle at the time he commenced.

At Bâle, at the time of my return, great was the number of those who practised medicine. Here is the list of the graduates: Dr. Oswald Ber, Physician to the City; Dr. Jean Huber; Dr. Isaac Keller; Dr. Adam de Bodenstein, called Carlstadt; Dr. Henri Pantaléon;[8] Dr. Gaspard Petri, called Mellinger; Dr. Guilelmus Gratarolus de Bergame; Dr. Jacob Huggelin; Dr. Jacob Wecker, the licentiate Philippus Bechius, and Joh. Bauhinus. I do not count Jacobus Myconius nor Dr. Jacobus Zonion who left after a short time. As to quacks there were: Ziliochs, of Saint-Alban, to whom one went to consult just like a physician, and the widow of Othon Brunfels who enjoyed a great reputation. To all these I added my own self and one year after, Dr. Theodorus Zwingerus[9]

[7] John Huber, of Bâle (1507-1571), a student of J. Sapidus, of Schlettstadt, studied more particularly at Montpellier and Toulouse. He practised medicine with success, was appointed professor of physics in 1544, a little later professor of theoretical medicine and in 1567, at the death of Oswald Ber, professor of practical medicine.

[8] Henri Pantaléon, born at Bâle in 1502, had frequently changed his profession and place of abode before being appointed, in 1544, professor of the Latin tongue at the Pædagogium, which did not prevent him from pursuing his studies in theology and medicine. Deacon of St. Peter, he obtained the licentiate in theology, but the ecclesiastical career did not appear suited to his character which was an enemy of constraint. After a time he gave up his functions as deacon and went to study medicine at Valencia, Avignon and Montpellier.

In 1558 the *concilium medicum* of Bâle received him in its midst. Pantaléon died March 3, 1595. Among his many writings may be mentioned his *diarium historicum* and the *Heldenbuch deutscher Nation.* Emperor Maxillian II made him Poet Laureate and also a palatin count.

[9] Theodore Zwinger, or Speiser (1533-1588), was a student of Thomas Platter and by his mother a nephew of the erudite printer Jean Oporin. He successfully occupied the chairs of Greek, Ethics and Theoretical Medicine at Bâle. It is said that his house had as tapestry only inscriptions in Hebrew, Greek, and German. Zwinger translated, at the same time adding commentaries, several works of Hippocrates and Galen, and composed among others, *Theatrum humanæ vitæ, Methodus apodemica* and *Physiologia medica.* His biography has been written by Felix Platter in the commencement of the *Theatrum,* in the 1604 Bâle edition. The account here given by Felix Platter is an honor to both these physicians.

swelled the list. Thus in 1557-1558, Bâle possessed nearly seventeen physicians. It was, consequently, necessary for me to strive if I were to make my livelihood; in this respect God has covered me with benedictions. At this time a certain Ammann was greatly extolled: he was a peasant at Utzensdorf to whom an extraordinary crowd rushed; the urine indicated to him the nature of the disease; during many years he performed curious practises which resulted in his making a very large fortune. After this individual the Jew Alsswiler was for a long time greatly sought after. In the *ruelle des Tanneurs* an old woman called Lülbürenen, also gave many consultations, likewise two executioners, Wolf Kaese and George Kaese; their elder brother had acquired a great renown as a physician at Schaffhausen, like his father Wolf, the executioner of Tubingen.

Patients from the middle class and nobility commenced to come to me. They submitted my knowledge to a singular test: they sent me their urine and I was to guess the disease. I did so well that several were greatly surprised at my replies and finally took the habit of consulting me. My clientele increased daily, not only in the city but also without. People came to Bâle for a stay to be under my care; others came and left at once, taking my prescriptions with them; or on the other hand, foreigners requested me to come to their houses and the castles; I went there with rapidity, hardly staying with them and regained my house as quickly as I had left. In this way it was possible to treat a large number of patients both near and afar.

In April 1559, a robber was to be tried: among other misdemeanors, he had broken into The White Dove, and taken away a wash tub. I begged my father-in-law, since he was member of the council, to have the cadaver placed at my disposal. Master Franz looked as if he thought my request would be rejected, because the University would claim the body; perhaps, also, he imagined that I would not know how to undertake a dissection. I was careful not to importune him further and I went to present my request to the burgomaster Franz Oberrieth. Although astonished in the first place that I should be desirous of undertaking such a labor alone, he evinced his good will toward me and promised to submit my request before the council the next day. On April 5, the criminal appeared before the court and was condemned to be decapitated. At the breaking up of the Council, my father-in-law came to tell me that the cadaver would be given over to me, which should be brought after the execution into the Church of St. Elizabeth, where I would have a permit to dissect it; only I was obliged to notify the doctors and barbers, so that they might witness the operation if they so desired.

Thus it was done. People of all conditions formed a numerous audience and I derived great honor from it because only a very long time before, not since Vesalius, had any public dissection taken place at Bâle. This work took me three days. I then boiled the limbs after they had been deprived of the flesh, I put them together, and had thus a skeleton that I still possess after fifty-three years. The mother of the robber was an over-seer of the women at the church of the hospital: many years had passed when one day she came to consult me. She had learned that the skeleton of her son was in my house; and in reality I had had a very nice show-case made for it in my room. This woman sat down on a bench quite near it, looked gravely at the skeleton without uttering a word; but when she went out she said to the people:

"Alas, will not one accord him a burying place?"

We now come to that portion of Platter's diary in which he describes the seven mortalities of Bâle, in other words, the seven visitations of the plague in this city. Although succinct, the description is most excellent and the statistics of deaths and recoveries are of very great importance, inasmuch as the figures demonstrate to what extent these ravages of former times went.

I remember that the first invasion of the plague occurred in 1539, 1540, and 1541, sometimes decreasing, at others redoubling its intensity. It lasted for three years, up to the end of 1541.

The second visitation of the plague took place during the years 1550, 1551, 1552, and 1553. It began towards the end of 1550, was extremely violent and killed many people. The following winter and even the spring time of 1552 were not so bad; nevertheless the scourge had not completely disappeared and in the autumn there was a very marked recrudescence in Great and in Little Bâle, which continued into April 1553.

The third plague, 1563 to 1564, was called The Great Mortality. It was extremely murderous although it did not last so long as the others. I had the opportunity of making myself useful to many people. The epidemic appeared in the winter of 1563; it extended up the Rhine and advanced to the Swiss countries; it disappeared towards the end of 1564, but it had time enough to carry away an extraordinary number of both young and old. Children were particularly afflicted, then the servants and workmen. Nearly all of those who, at the Saint-Jean, came back from foreign service, succumbed. The hospitals and the refuges were filled with the sick; among the middle class there were many victims, merchants and artisans, counsellors, savants, students, scholars and preachers. Pregnant women and those who had been delivered died for the most part. Likewise elderly people. At times, and I witnessed it, as many as twenty bodies were buried at once in the same ditch. The dead were transported without interruption from St. Elizabeth's hospital and were thrown into a large ditch; the latter remained open for several days until it had been well filled, and the bodies were only covered over by a very thin layer of earth. The streets were completely deserted; in the assemblies, at the churches and elsewhere, considerable emptiness prevailed and a number of widows and widowed were to be noticed. However, cases of cure after a long illness were far from being infrequent.

Although large, the number of victims is uncertain, because the deaths were not registered as was the case some years later. Thousands and thousands of deaths were commonly stated; this is an evident exaggeration. Dr. Sultzerus, at that time the first pastor, and myself who had to care for a large number of patients and who took notes of the deaths, we have, by calculating each on his own account, estimated the number of deaths at very nearly four thousand; for Bâle this can hardly be counted as small. At the hospital, according to the expenses of burial inscribed on the register from Februray 28, 1564 to March 24, 1565, I calculated that during this period the number of deaths must have been exactly two hundred.

As soon as the contagion was on its decline, and even while it was in its full blast, carrying away entire families, marriages continued to be contracted in full force. People remarried a few weeks after having been widowed; pregnant women, even nearly at their term, contracted second marriages, and the authorities were obliged to prevent them from taking a husband until a certain number of months had elapsed; widows and young girls were also ordered not to marry a stranger who was not a bourgeois, under the penalty of being expelled from the city.

The fourth mortality took place in 1576, 1577, and 1578. It broke out at Augst in the rue Blanche in 1576 at the house of a messenger who had brought it back with him from some unknown spot and who with his wife was the first victim, without counting that eight days later his brother-in-law and brother were in their turn seized upon. The plague spread from house to house and street to street, and soon it had invaded Augst and Bâle. It continued during the entire year of 1577, developing with more or less severity, sometimes here, sometimes there, up to the

THE ARMS OF PLATTER.
After a painting on glass at the Bâle Museum.

FELIX PLATTER, ANNO ÆTATIS 48.
After a portrait painted in 1584 by Hans Bock of Bâle.

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spring of 1578; then it ceased. During these two years the number of victims was quite large.

The fifth mortality occurred in 1582 to 1583. It commenced towards the month of July 1582 and lasted into March 1583. During this short lapse of time it carried away many people, about one thousand and ninety-five individuals. The records of the hospitals showed me that from July 1582 to March 1583 one hundred and three people died, the larger number from the plague; it also shows that the total number of recoveries was one hundred and fifteen. At St. Peter, eleven people were buried in July, twenty-five in August, twenty-eight in September, thirty-nine in October, thirty in November, thirty-one in December, and twenty-two in January and February, 1583.

The sixth mortality appeared in 1593 and continued until the end of 1594. How many people were afflicted in this epidemic? This is a point upon which nothing absolute can be said, although it was in this very year that a record of births and deaths was commenced, these records being read on New Years' Day after the sermon of the evening. Five hundred and twenty-four people died in 1593 and nine hundred and two in 1594. If from these figures one deducts the average mortality in normal years, viz., two hundred and fifty, it may be supposed that in 1593 the epidemic carried away two hundred and seventy-four persons, and six hundred and sixty in 1594; total: nine hundred and twenty-six persons, both young and old.

The seventh mortality (1609, 1610, 1611) commenced in October, 1609. The plague was already present in the country of the Margrave, particularly at Loerrach, likewise in several places in Alsace; It appears that the apprentice of the baker Algenburg contracted it at Schopfen, where everyone was dying, and brought it back to the house of his master who lived in Little Bâle. In the first place, neither the ordinary symptoms of the scourge nor the head-ache made themselves felt, so that little attention was paid to it, although in Great and Little Bâle the number of patients and deaths was from time to time greater than usual. There was even doubt that it was the plague, in spite of the characteristic symptoms which appeared here and there; but in July the epidemic declared itself frankly and with an increasing violence. From October 12, 1610, from two hundred and fifty to two hundred and eighty-eight people were buried each week; finally in December the scourge decreased to about one-half and even more.

There were:	No. of cases	Deaths	Cures
In the five faubourgs	1720	1146	574
In the rest of the city....	2990	1913	1077
In Little Bâle	1039	724	315
At the hospital.....	659	185	474
Total	6408	3968	2440

In completing this recapitulation by means of the records of Saint Theodore and of the hospital, I find the total number of deaths comes to four thousand and forty-nine; there were one hundred and sixty-five families in which both the husband and the wife died.

TUBERCULOSIS IN INFANCY AND CHILDHOOD.*

By Henry Koplik, M. D., New York.

Tuberculosis is a disease not only prevalent and widely so in infancy and childhood, but is peculiar to this age. At this time its prevalence is widespread and it presents features so diverse from the same disease, as it occurs in adult life, that its study is of deep and startling interest. It is quite in accord with the pleasant changes of time and place that this subject should be considered before a society which bears the name of one of the great bedside observers of modern times. Lænnec was among the first to call attention to the unity of some of the forms of this disease in infancy and childhood with tuberculosis. Scrofulosis that syndrome peculiar to children was recognized by him to be nothing more or less than a form of tuberculosis.

I find it then appropriate that any analysis of this disease should take into consideration his great influence and should be the subject of an address before this distinguished body. The study of tuberculosis in infancy or childhood reveals its universal prevalence at this time of life, and lends support to the feeling that tuberculosis or its forms which affect adults or adolescents must, in a vast majority of instances, date from childhood. Moreover, a study of the disease in early life teaches forcibly the vast strides made in modern medicine through the study of pathology and experimental medicine. No disease illustrates this more completely than tuberculosis and no disease can show more enlightenment than tuberculosis in infancy and childhood through animal experiment. We can almost duplicate most of the forms of tuberculosis in infancy and childhood in the experimental laboratory. Through the work thus done and the light shed upon certain phases of the disease by experimental work we, to-day, feel more willing to explain hitherto obscure features of the disease and the reaction of the body cell against its essential cause, the tubercle bacillus. The clinical recognition of the various forms of tuberculosis in infancy and childhood has crystallized with greater certainty than even a decade ago at the bedside. Tuberculosis takes on phases and forms in infancy and childhood, and the infant organism reacts to the tubercle bacillus in quite a different manner from that of the adult. We will show that this is due to the soil in which the disease finds itself as distinguished from the adult and that the adult forms are distinctly peculiar and different clinically from the forms of childhood for distinct and experimentally proven reasons. No age is exempt from tuberculosis, and it is needless to assume any proposition tending to prove the contrary.

Much has been said and discussed concerning a so-called "disposition" to tuberculosis (von Behring, Ehrlich, Hamburger, Cornet). It cannot be said that infants or children are predisposed to tuberculosis any more than they are to measles or diphtheria, but one can say that, given an exposure to infection or the elements of infection they will contract tuberculosis, and also that they are in a position more than any one else to be exposed. They crawl along the floors, they are among

* Paper read at a meeting of The Lænnec, a society for the study of tuberculosis, The Johns Hopkins Hospital, January 29, 1912.

the poor crowded in with the tuberculous and phthisical; they put all things in their mouths, and their food—not milk alone—but other foods, such as candy, are more likely to come in contact on account of the habits of the poor with tuberculous material. Every child, therefore, infected with tubercle bacilli becomes tuberculous, and it may be said the disposition to contract infant tuberculosis is ever present in every child. Of course, the course of the infection will vary with the amount of infectious material introduced into the body and the individual disposition of the subject. Thus it will be shown that in certain individuals, as in very young infants and children, the tuberculous infection will run an acute course, in others a peculiarly protracted course (scrofulosis), and in older children the course of the disease will approach the forms seen in the adult.

We know that tuberculosis can be congenital not hereditary (von Behring), and we know that the infective agent may pass from the blood of the mother through the placenta into the body and organs of the fœtus. That tubercle bacilli have been found in the maternal placenta (Schmorl and Geipel), is well established beyond a question of a doubt, and that the bacilli can be found in the various organs of the fœtus with or without the formation of the tubercle is also proven (Rietschel, Sitzenfrei). That the fœtus can be born tuberculous and harbor tubercle bacilli and not manifest any of the signs or symptoms of tuberculosis is now an accepted fact (Baumgarten). It is true that in very early infancy, the first three months, there is an evident hiatus in the occurrence of tuberculosis, but we understand that this is so not because these infants are not tuberculous, but because at this period the tuberculosis may be inactive or latent. It is not necessary to assume that the sperma cell can carry tubercle bacilli or tuberculous poison to the ovum; this is a negligible factor in the face of all the possibilities which are mentioned from the maternal side.[1] Up to the second year of life, the incidence of active tuberculosis is less than at any other period. It increases from this time on and some authorities think that the time of greatest incidence of infections takes place at the fourth to the sixth year of life (Hamburger). The percentage of tuberculous children increases steadily up to the fourteenth year of life.[2] The course then takes a downward trend to adult life. Thus not only do the acute forms of tuberculosis diminish in later childhood, but the more chronic forms appear at this time proving that not only is tuberculosis chronic and curable in the sense that it annihilates itself, but that some of the forms are carried from later childhood and adolescence into adult life, where, on account of certain well established facts, tuberculosis takes on different forms from that found in children.

[1] Jani found tubercle bacilli in the genital organs of men suffering with tuberculosis. That bacilli can be carried into the uterus and adnexa has been demonstrated by animal experiment (Gaertner and Sitzenfrei). Tubercle has been found in the placenta of tuberculous women not necessarily in the advanced stage of the disease (Sitzenfrei, Schmorl).

Tubercle bacilli or tubercles have been found in the placenta, cord, decidua, fœtus and liquor amnii (Schmorl).

Congenital tuberculosis may occur in infants who have lived six months after birth (Rietschel, Sitzenfrei), and the infection can occur at any period, more probably toward the end of pregnancy in most cases. Cases of congenital tuberculosis have been published by Birsch Hirschfeld, Aschoff, Rindfleisch, Lehman, Schmorl, Kockel, Thierclin, Andrews, Hamburger, Sitzenfrei, Rietschel and Wollstein.

The infection from the mother through the ovum may be rejected, it takes place through the blood and placenta. This applies not only to tuberculous changes in the fœtus but in infants who die within the first half year of life.

Cases of congenital tuberculosis are certainly unusual and those in the first three months of life rare. I call attention to my early cases of tuberculous meningitis and the case of tuberculous peritonitis in an infant 4½ months old in whom tubercle bacilli were found in the fluid of the peritoneal cavity in large numbers.

Frequency.

The frequency of tuberculosis in infancy and childhood has been approached by various observers in various ways. It is quite evident that the results of autopsy are the most certain evidence, for here we can establish not only the healed or inactive or even the truly latent cases, but also the cases of active lethal tuberculosis. But autopsy material gives only a relative view of its frequency in the various strata of the population. Autopsy shows only those cases which have been in hospitals. Again one can approach the subject from the side of the district or family physician. This also has many possibilities of error for some physicians may not diagnose a case or conceal a diagnosis even should a census be taken of all individuals in any district. The modern methods of tuberculin diagnosis have enabled us to form an idea of the great prevalence of tuberculosis, but here again the material is drawn not from the population at large but from the dispensaries and hospital clinics. With these points well before us let us see the results of autopsy statistics as they are given to us to-day.

Taking large numbers of autopsies it is evident that the percentage of incidence will vary according to the number of autopsies. Thus in 16,581 autopsies Froebelius found that the first year of life showed an incidence of 2.5% of tuberculosis, the 123 autopsies of Harbitz 20.3%, Albrecht recorded 1300 autopsies with an incidence of 14.5%, Hamburger, 276 autopsies in the first year of life with an incidence of 4.5%, but none before the sixth month. Most interesting are the statistics of Hamburger taken from the autopsies made by Ghon at Escherich's clinic in Vienna. Taking 617 autopsies, tuberculosis was an accidental find in 17% of the cases in which the ages ranged from early infancy to the fourteenth year. These children died of all causes, and it is interesting that in them the accidental find of tuberculous lesions increased from 17% in the second year to 53% of all the cases in the 11th to 14th years, thus bearing out the assertion previously made that in adolescence the number of cases which carry their tuberculosis into adult life increases, especially from the seventh year.

[2] Naegeli, Hamburger.

Taking all autopsies of Ghon, 848 cases, the following table is instructive:

0- 3 mos.	105 cases of which	4%	were tuberculous.
4- 6 mos.	73 cases of which	18%	were tuberculous.
7-12 mos.	140 cases of which	23%	were tuberculous.
2 years	179 cases of which	40%	were tuberculous.
3- 4 yrs.	175 cases of which	60%	were tuberculous.
5- 6 yrs.	67 cases of which	56%	were tuberculous.
7-10 yrs.	65 cases of which	63%	were tuberculous.
11-14 yrs.	44 cases of which	70%	were tuberculous.

It is doubtful whether other great cities will show such a very marked preponderance of tuberculosis, and in fact there is reason to believe that they do not. In America the incidence will not be so great, for I do not believe from my studies that our poor are so badly nourished or so severely crowded as in Vienna. For the present it seems that other large cities of Europe as Zurich (Naegeli) show a very high percentage of tuberculosis as compared to Vienna. In the Charité at Berlin and the Berlin Orphan Asylum, Finkelstein calculates that of 5600 children of one year of age 72 are tuberculous.

Another way of gaining an insight into the frequency of tuberculosis in infancy and childhood is by means of the tuberculin skin reaction of von Pirquet and the *Stich* reaction of Epstein, Escherich and Hamburger. Epstein was, I believe, the first to call attention to the fact of the lack of reaction in the new born to tuberculin, and at the same time noticed the very important phenomenon of the *Stich* reaction, but it remained to von Pirquet to simplify the tuberculin reaction so as to nullify its ill effects and for Hamburger to point out that in those cases in which the cutaneous skin reaction of von Pirquet failed the *Stich* reaction might succeed and therefore was the most positive and delicate of all reactions, but more of this later.

von Pirquet took 988 children frequenting the Escherich clinic and found the following incidence of reaction to tuberculin:

0- 3 mos.	0%	2- 4 yrs.	37%
3- 6 mos.	5%	4- 6 yrs.	53%
6-12 mos.	16%	6-10 yrs.	57%
1- 2 yrs.	24%	10-14 yrs.	68%

Of 693 cases of inactive tuberculosis, that is children not suffering from symptoms of tuberculosis, he found 55% at the age of 10 to 14 years.

0- 3 mos.	0%	2- 4 yrs.	13%
3- 6 mos.	0%	4- 6 yrs.	17%
6-12 mos.	3%	6-10 yrs.	35%
1- 2 yrs.	2%	10-14 yrs.	55%

Thus one-half or more of the children (55%) of the poor who frequented the clinics for all causes other than tuberculosis, were tuberculous, that is, had tubercuous foci. Hamburger's statistics are still higher because he took the negative cases of von Pirquet and injected them with tuberculin and found that many of the children who did not respond to the cutaneous test did so to the *Stich* reaction. He found that between the 12th and 13th year fully 95% of the children of Vienna, among the poor, were infected with tuberculosis. Ganghofner of Prague obtained as high as 70% of infections. Hamburger states that the children of the poor are so situated that at puberty possibly all are infected with tuberculosis. If this statement may appear startling and in future found not to be quite apt, still it illustrates the main keynote of my theme, the startling prevalence of tuberculosis among the children of the poor in the large cities of the world.

The avenues or modes by which the tubercle bacillus may gain access to the body has been a subject of bitter controversy. It is not as yet absolutely established that this phase of the tuberculosis question may not receive additional light from future work. Until a recent date it has been accepted that aspiration or the aerogenous way was by far the most frequent avenue through which the infective agent entered the body (Weigert). Strength was lent to this theory by the fact that in a vast majority of cases, at least in children, the lungs were found involved. In recent times through the writings of von Behring and Schlossman light has been thrown upon the modes of infection through the digestive tract or deglutition.[3] In the heat of discussion this has been misinterpreted in some quarters to mean that von Behring especially emphasized the rôle played by cow's milk in causing tuberculosis in children. This is not exactly so. Schlossman has taken pains to point out that in supporting the theory of infection through the digestive tract, he includes all infectious matter entering the mouth, pharynx, œsophagus, stomach and intestines. This would include not only infected food but sputa in a moist or dried state adherent to objects, or anything which would introduce such infection, such as kissing, playing with toys infected with sputum, and foods. Schlossman contends, and this has been proven and accepted, that bacilli in the very young may thus enter the stomach and intestines, and, especially in infants, pass through the very permeable mucous membrane into the lymph circulation, leaving no trace, and from thence to the vena cava to be finally deposited in the end capillaries of the lung. It will be seen that this is an entirely different matter from the contention that through milk alone tuberculosis is in any appreciable percentage of cases a cause of infantile tuberculosis. All are agreed that the human subject is the main source from which emanates all tuberculous infection. In Vienna, Escherich and his school were at pains to prove that in a great percentage of cases infection could be traced to a person infected with tuberculosis who had been in the immediate vicinity of the infected child. It seems from a close study of my own experience in New York that I can give my unreserved support to this contention. I have been able to trace over and over again tuberculosis in parents as well as children and I have had several children under my care with symptoms of glandular, pulmonary and brain tuberculosis whose parents were either actively or inactively tuberculous.

It may be laid down as a fact that infection through tuber-

[3] Bartel and Spieles come to the conclusion as a result of animal experiment that infection by deglutition (dirt and smut) is the most frequent mode of contraction of tuberculosis in children.

culous milk, that is, not milk containing human tuberculous matter, but milk from tuberculous cows is rare. Such tuberculosis cannot form over one to two per cent of all the cases of tuberculosis that we know of, if indeed it reach that percentage. Since it has been possible to identify bovine and human tubercle bacilli, only 41 cases could be collected of tuberculosis in children caused by the bovine bacillus (Hess). The cases were drawn from all over the civilized world.

In this connection it may be of interest to note that the mode of feeding as shown by the investigations of the Phipps Institute has little to do with the implantation of the tubercle bacillus in the human subject. Of 665 cases of tuberculosis in adults, 90.9% were breast fed in infancy and only 9.2% bottle fed. The peculiar features of tuberculosis in infancy are especially emphasized by a study of its pathologic anatomy.

A very striking peculiarity of the pathologic anatomy of tuberculosis in infancy and childhood is the preponderating involvement of the lymph nodes and especially those of the lungs. Weigert was first to point out this fact and I remember that Prudden never tired of demonstrating it at autopsy. They are involved in fully 80% to 90% of all cases of tuberculosis in infancy and childhood. Ghon found that in Vienna the autopsies on children from Escherich's clinic gave as high as 98% of frequency in the involvement of these glands. When involved a primary pulmonary focus could always be demonstrated (Escherich, Kuss, Albrecht). Some have contended (Kuss) that they could demonstrate in these cases a port of entry in the tracheal mucous membrane. Others (Albrecht) demonstrated to their satisfaction that this primary focus in the lung existed in the lymphoid bodies of the fibrillar connective tissue of the lung. It may be accepted apart from the above that in tuberculosis of the bronchial lymph nodes, the primary lesion is in the lungs (Baumgarten). The peripheral lymph nodes are less often affected though in diseases of the pleura and apices of the lung the supraclavicular nodes may be involved and palpable (Finkelstein).

Primary tuberculosis of the tonsil is rare in infancy and childhood. Of 32 cases of tuberculosis of the tonsil Geipel proved that the primary infection was in all probability to be found in the lung in 13. I have published one case without autopsy in which the involvement of tonsil was the first *clinical* evidence of the tuberculous process in an infant, but I admit that in this case autopsy might have revealed a primary focus in the lung. The infant had been in the vicinity of phthisical people for some time.

Meningitis which is a general miliary tuberculosis, and is of great frequency in infancy and childhood, is peculiar to this period of life and of preponderating frequency as compared to the adult forms of tuberculosis. It is a hæmatogenous infection in most cases. Tuberculosis of the pericardium is rare and that of the larynx and trachea is always secondary.

The great infrequency of cavities[4] in the lungs of children as compared to that of the adult has been remarked upon especially by Hamburger and von Behring. In infancy Hamburger explains this by the fact that as in the experiment the guinea pig who has been repeatedly infected with a weakened virus may develop cavities in the lung, so the adult shows this tendency to cavity formation because his phthisis develops on a soil previously infected in infancy and childhood. The main reason, however, clinically is that in the infant and child infected up to the sixth year tuberculosis may and does run a rapidly acute course, thus allowing for cavity formation only in cases of slower course later in childhood.

[4] Cavities are not so infrequent in infants, and according to Aronade, Geipel found them in 8 of 30 cases, Finkelstein in 40% of his cases and Hohlfeld and Querin met them but rarely in the upper lobes of the lungs.

Clinical Features.

The clinical features of the various forms of tuberculosis in infancy and childhood are characteristic of this period of life and some of the forms are peculiar to infancy and childhood. The course of the tuberculous process under the fifth year of life is acute and even in the pulmonary cases the duration of the illness is quite short as compared to the chronic course of the disease prevalent in the adult. In the nursing infant the symptoms are often obscure and become evident only in the terminal stage of the disease. The initial period of the disease may run its course without fever. An obscure febrile movement with a temperature ½ to 1 or more degrees daily above the normal for weeks or months is quite characteristic of some forms of tuberculosis in infancy and childhood. I have recently seen a case of a boy of seven years of age who for years suffered from tuberculous adenitis, having been operated upon twice, who ran a low temperature of a degree or a degree and one-half above the normal for two years after operation.

I have for the purposes of this paper collected all the cases of tuberculosis coming to my hospital service in the past five years. Those before 1907 were only tested with the tests prevalent at the time. Others have been carefully confirmed both at the bedside and in the laboratory so that it is hoped a quite accurate résumé of the cases is given.

There were 209 cases in five years, dividing themselves as follows:

Tuberculous meningitis	158 cases.
Tuberculous pleurisies	23 cases.
Tuberculosis of the lungs	17 cases.
Tuberculosis of the peritoneum	8 cases.
Tuberculosis of other organs	3 cases.

It is not the intention of this address to take up anything but the broad features of the various forms and manifestations of tuberculosis, and, for this reason, when we consider sets of cases I shall limit myself only to striking features in the course of the disease.

It is first noticeable that the meningitic form of the disease is, *per se,* the one most looked for at the bedside. Of the total of all my cases, 75% took this form, bearing out in this respect the acute nature of the disease, the miliary form. It must not be forgotten that a large number of cases of meningitis are really terminal manifestations of a focus of tuberculosis long dormant. The history of this disease in many children bears

out this assertion. I have only to recall that in many cases of bone tuberculosis meningitis is the terminal stage of the disease. It is only in very early infancy and childhood that we see the disease burst forth after a preliminary short illness. Of my cases of meningitis fully 122, or 80%, occurred in infants and children below the fifth year of life. I had two infants stricken with the disease at the age of four months and one at 13 weeks. Some authors might be prone to trace the infection in such cases either close to the period of birth or even before it. Such is only speculation. There were 22 cases during the first year of life of the total of 158 cases, 14%. In many of these cases I could trace, in the history, the infection to the immediate vicinity or family of the patient. What a commentary on modern prophylaxis and what a sad lesson to parents should they for a moment understand the true state of affairs. Thus below the fifth year of life the most frequent form of tuberculosis is the miliary or, *per se,* the meningitic form. Later in childhood the miliary form of tuberculosis causes great uncertainty at the bedside. I cannot forget the cases of obscure fever which range from 103° to 105° F. to the normal with clear sensorium, with an apparent previous history of freedom from disease. In these cases the temperature range extended over two or more weeks with a negative von Pirquet reaction until the clear sensorium gradually became clouded and the patient passed into sopor and insensibility with all the signs of meningitis. Such cases cannot, because of the absolute absence of lung signs, except in the terminal stage, be differentiated from other forms of continued fever such as typhoid fever. The question of differentiation between typhoid fever and acute miliary tuberculosis is always a difficult one in later childhood, the fifth to eighth year. Not only the von Pirquet but also the Widal reaction fails us in many of these cases.

A study of my cases of tuberculosis of the lungs in infancy and childhood shows that here also the disease often runs an acute course. The physical signs at first simulate an ordinary broncho-pneumonia. The temperature, however, is continuous past the period of an acute broncho-pneumonia. The signs localized in most of my cases to the apices of the lungs on one or both sides, persist, fail to resolve, the emaciation, the failure of circulation (cyanosis) will raise suspicion at once of the tuberculous nature of the disease. If added to this there is a cough of a rasping, metallic nature and so-called expiratory dyspnœa, our doubt develops into certainty. Many of the pulmonary cases show glandular involvement in the form of enlarged supra-clavicular lymph nodes. Others show a stubborn diarrhœa. Many cases, especially those in later childhood, run a chronic course very much the same as in the adult. Hæmoptysis is not as frequent as in the adult. I have not met it in infants but have seen it in later childhood and then it was a precursor of rapid spread of the disease. The acute miliary form of lung tuberculosis occurs not only in infancy but in later childhood. I still cannot divest myself of the influence of the teachings of my master Henoch when I hestitate to diagnose clinically enlarged bronchial glands which, even with the X-ray, seem very difficult of diagnosis. It is true that in fully 80% to 90% of autopsies there is an enlargement of the bronchial lymph nodes but their diagnosis at the bedside, in spite of the teachings of the Vienna school, must be made with great caution. It looks too much like a forced attempt at making a pathological entity fit a clinical picture. Of the 17 cases of pulmonary tuberculosis all were below the age of three years, thus accounting for the acuity of the progress of the disease.

To me as a clinician the greatest interest centers in the cases of dry pleurisy and pleurisy with effusion which we meet in children who have not presented any symptoms of a previous pulmonary affection. What proportion of these cases are tuberculous? This is not only an important question but one which in practice brings us face to face with the necessity of action in regard to the future well-being of the patient. What kind of pleurisy is really of tuberculous nature in children? This question is best answered by looking over carefully sifted material of my hospital and private practice. In my hospital service during the past five years there have occurred 45 pleurisies. Twenty-three of these (50%) were manifestly tuberculous, sixteen were metapneumonic, seven occurred in subjects suffering from rheumatism and heart disease, and one in a nephritic. These statistics exclude all cases in which the effusion was not clear and serous macroscopically. As to age in the tuberculous cases 7 were below the age of 5 years, the remaining 16 ranged up to the 13th year. I think we may regard a pleurisy as tuberculous whose onset is not stormy though it may be acute or sub-acute, in which the temperature is not very high, 102°, 103° or even 104° F., in which the effusion is clear and absolutely free from organisms, in which there is a loss of flesh and strength and in which there is a history of tuberculosis in the vicinity of the patient, and in which there is a positive result to the tuberculin tests, either of the skin or subcutaneously. From this it will be seen that by no means can I regard the assertion of some (Hamburger) as true that almost all pleurisies in childhood, especially those with serous pleurisies between the ages of 2 or 3 years, are tuberculous.

We have found many metapneumonic pleurisies at this age with serous exudation in which there was a distinct preceding history of broncho-pneumonia and in which the exudate showed microorganisms. I think my figure of 50% of frequency of tuberculous pleurisies in infancy and childhood will be found nearer the truth.

In those cases of tuberculous pleurisy in which a blood count was made and in which a positive tuberculin reaction either of the skin or subcutaneously was obtained there are the following features.

The number of white blood cells in sixteen tuberculous cases ranged from 1100 to 20,000 to the cubic millimeter and the polynuclear leucocytes from 51% to 85% so that this gives us but little to serve as a guide.

More interesting is the cytology of the fluids obtained from the chest. In those cases in which such an examination was

made or was possible the lymphocytic nature of the cells in the fluid was quite apparent, in the tuberculous cases the lymphocytes ranged from 90% to 100%, this in the absence of any bacteria seems to me worthy of note.

In all the above I have absolutely disregarded all pleurisies which have suggested purulent exudate and only considered those in which the effusion was clear.

I have recently seen two cases in older children with a dry pleurisy extending over weeks not giving any symptoms but a mild hacking cough and still refusing to react to tuberculin. Such cases, I think, can well be traced to influenza or preceding broncho-pneumonia.

The importance of a definite decision in these cases cannot be overestimated as a pronouncement of tuberculosis means the breaking up of home or business, even among those of moderate means.

In discussing tuberculous peritonitis, I wish first to call your attention to the remarks of Heubner on intestinal tuberculosis in which he makes note of some of his cases occurring in infancy as also of tuberculosis of the mesenteric glands.[5] I have rather preferred to give a résumé of those cases in which the prominent symptoms were those of a tuberculous peritonitis. Of eleven cases, six presented complications in the lung, some cases were the miliary form, others the kind in which the formation of masses in the abdomen prevailed. The youngest case was twenty-two months of age; the older children ranged from ten to twelve years. I have seen a baby in private practice 4½ months of age with tuberculous peritonitis. It is my impression that the peritonitic form is not as frequently met with as other forms of tuberculosis in infancy and childhood.

I wish to call your attention and engage your interest in the remaining forms of tuberculosis. I refer to the form which for eras in medicine has been the source of much contention and discussion—this is the so-called scrofulosis. Some pediatrists who wish to be in the van of progress have, I think, prematurely suggested striking the word scrofulosis from our nomenclature. Lænnec was the one who first rescued the term from opprobrium and established the connection with tuberculosis of the glandular form of scrofulosis for all time. It is interesting to see the tenacity with which some of the great minds in pediatrics have clung to the idea that all scrofulosis is not tuberculous though they admit that scrofulosis may become tuberculous (Henoch). It would scarcely interest you to recite all the various authorities, Henoch, Heubner, Cornet, Escherich, Czerny, who have taken part in the discussion of what really constitutes scrofulosis. Allow me to say that with recent advances in our methods of diagnosis, we are fast beginning to recognize that in the term scrofulosis there is a distinct clinical tuberculous entity. I think for my part that the picture is so definite that it would be a pity to discard it, especially as it is a syndrome definitely peculiar to infancy and childhood. Escherich who has given this form of tuberculosis much thought comes to the conclusion that scrofulosis is a form of infantile tuberculosis which develops on the foundation of a lymphatic constitution. What is a lymphatic constitution? may be asked. It may be characterized as a tendency from earliest infancy to a hyperplasia of adenoid tissues in the body, *adenoides Gewebe*. These lymphatic children show enlarged tonsils, adenoids in the retronasal and pharyngeal space, enlarged lymph nodes throughout the body, and hyperplasia of the mucous membranes. Even in the intestines there may be an enormous hyperplasia of the solitary follicles in the whole extent of the small and large gut. The thymus gland is enlarged. Such children are anæmic and of a pasty complexion, they suffer from catarrhs of the mucous membranes and in many of them we have cyclic albuminuria. If upon such a soil there is implanted an infection with tubercle bacilli we have an especial vulnerability and over sensitiveness to external traumatism and the development of an allergie against minimal doses of tuberculotoxin. We have as a result, the development of skin eruptions in the form of scrofulides or tuberculides and later through the lymph and blood the formation of localized tuberculous foci or generalized tuberculosis. The clinical picture of scrofulosis is quite characteristic: the glandular enlargements in the form of tuberculous adenitis, catarrhal states of the conjunctivæ, the nose and respiratory tract, the affections of the bones, spina ventosa, osteomyelitis of the long and flat bones, including those of the skull, manifestations on the skin in the form of lupoid eruptions, ecthyma, tuberculides and scrofulides, and all affections of the various structures of the cornea and lens of the eye. All these focal inflammations do not always lead to death; they are slow to develop and tend to break down (glands) and suppurate, calling to their aid the mixed infections; they have a tendency to heal. Here is a distinct set of syndromes not seen in adult life. Occasionally we see isolated forms of the above inflammations in one patient. It is not uncommon to meet a tuberculous adenitis in an otherwise healthy looking child, or the tuberculous gland at the angle of the jaw may be combined with enlarged tonsils. Again an eye affection may for a time be the only focus apparent, or a hidden focus in a bone, as, for example, in the head of the tibia may be the only symptom in the patient, and then apparent only by the X-ray. As a rule, however, the typical scrofulous child is anæmic though well nourished; there are catarrhs of the conjunctivæ and nose, with enlarged glands about the neck, and the skin, as stated, shows eczematous tendency with or without tuberculides or ecthymata. In two infants recently under my care there were foci in the lung. I am inclined to believe that this is certainly a definite entity, and if I may theorize as others have, it is the result of repeated infections with minimal amounts of tubercle bacilli,

[5] There is a great discrepancy in the statistics of various investigators as to the frequency of primary intestinal tuberculosis.

Some put it at 0.9% of all tuberculous children (Baginsky) others as high as 47.6% (Edens) and some even at 16 to 20% (Beitzke).

In England Price Jones places the frequency of tuberculosis of the alimentary tract as high at 25% of all the cases of tuberculosis in children.

so that there is developed an active immunity against rapid advance of the disease. It may be as Escherich says that such a form of tuberculosis presupposes a lymphatic soil. At all events scrofulosis is an interesting entity, and I am not at all prepared to part with the term. It is in short the lymphatic form of tuberculosis.

The Diagnosis.

In the vast number of cases there is no difficulty outside of clinical perspicacity in surmising the diagnosis of tuberculous processes in infancy and childhood. The great advances in aids to diagnostic precision in the past ten years can only be appreciated by a study of the writings of a past decade and those of to-day. The uncertainty which at times is reflected in the writings of the master mind, Henoch, is not found in the works of the writer of to-day. This change has been made possible through a simplification of our ideas on the unity of the various pathological forms of tuberculosis not only confirmed at the autopsy table but in the bacteriological experimental laboratory. In the various forms of meningitis there are few difficulties in certain classes of cases. It is in the early stages of tuberculous meningitis that difficulties arise. I have recently pointed out that the differentiation of forms of encephalitis from those of meningitis gives rise to great and at times insurmountable obstacles.[6] In these cases the tuberculin reactions leave us if positive, in doubt; if negative, they are of value, and yet, as in other diseases the whole picture clears up as the disease progresses. Tuberculin reactions must be interpreted in light of clinical symptoms. The simplicity in the technique of tuberculin reactions has been due to the era-making work of Escherich, von Pirquet and their pupils, of the Vienna school. It has been shown simply by means of harmless technique that tuberculosis is one of the most prevalent of diseases among infants and children. At the same time it has also brought us more and more power over the remedy tuberculin than ever before. If some methods of using tuberculin such as the *Stich* reaction of Epstein, Escherich and Hamburger, and the cutaneous reaction of von Pirquet are harmless, especially the latter, we have learnt the dangers of other methods such as the ophthalmo-reaction of Wolff-Eissner. In the clinic, at the bedside, the mode of using tuberculin by preference is that of von Pirquet. If this leaves us in doubt we may make use of the *Stich* method of Hamburger. In this last method caution must be exercised until we become acquainted with the smallest dose of a tuberculin solution (O. T.)[7] beginning with 1/10 of a milligram and increasing the dose gradually up to 1/4 milligram which will be borne by the patient. I rarely pass beyond this. I will not here dilate on the peculiarities of the negative reactions, or so-called late reactions (*spät Reactionen*). This can be found in the writings of von Pirquet to which we cannot add anything, so classic have been the observations. I wish, however, to call attention to the negative reactions in the later stages of meningitis and lung tuberculosis, and also advanced miliary tuberculosis of the body and peritoneum which we have had abundant opportunity to confirm. In the cases of so-called scrofulosis the reaction and induration is in some cases simply enormous. The induration persists for a long time. The allergie in these cases is certainly exceptional, and is awake to an infinitesimal amount of tuberculotoxin proving that here we have a condition *per se* characteristic. Escherich called attention to this in these cases. In other words there was an increased immunity. Escherich explained also the skin eczema and lesions seen in these subjects on the theory that the secretions of these patients contained the tuberculotoxin, and when a scratch or wound of the skin was exposed to the action of the secretions of the patient a species of autoinoculation took place, an allergie was immediately manifest; hence, the recurrent inflammation of the skin in scrofulous patients.

I wish to call attention to a phenomenon which must have been evident to others. In tuberculous pleurisy of children, in whom a von Pirquet test has been performed, and a positive result obtained, it is well not to try the subcutaneous method of diagnosis, for the confirmation of the local nature of the tuberculosis, unless we are prepared for a recrudescence of symptoms. In two cases of pleurisy with effusion in whom a positive result was obtained by the von Pirquet method, I injected tuberculin to see first whether I could obtain a *Stich* reaction and whether there would be a rise of temperature. I obtained both but with them an increase in the fluid which had begun to absorb and an exacerbation of the local subjective and objective signs. In both cases the results were disquieting, especially as I regard the course of such pleurisies in children, even if tuberculous, as benign and with a tendency to spontaneous resolution, so that the recrudescence of symptoms in these cases seemed to be a warning not to persist in

[6] I wish to emphasize the fact that in tuberculous meningitis the careful study of the fluid obtained by lumbar puncture is of the highest importance. In the second edition of my treatise on the Diseases of Infancy and Childhood, 1906, and also in the third edition, I laid especial stress on the cytology of this fluid which showed a predominance of mononuclear cells.

In one case there was an equal number of mononuclear and polynuclear cells. The predominance of mononuclear cells is so constant in this disease as to be a characteristic, but not absolutely pathognomonic, element in the fluid obtained by puncture in cases of tuberculous meningitis apart from the presence of tubercle bacilli. In 13 of 14 successive cases clinically diagnosed as tuberculous meningitis in my wards Bernstein (Koplik, second edition, 1906) found tubercle bacilli in 13.

In the years 1904 to 1906, 29 cases diagnosed as tuberculous meningitis revealed tubercle bacilli in the fluid of puncture in 24. In two of these 29 cases a diagnosis was not fixed positively at the time of puncture. Thus in 24 of 27 cases punctured, tubercle bacilli were found as confirming the clinical diagnosis.

In some cases the bacilli were found only after death and I think this success was due to sedimentation post mortem of bacilli in the lower portion of the spinal canal.

These facts have convinced me that in all cases if the search were painstaking the bacilli could be found.

Holt recently, in a paper on meningitis, has confirmed this constancy of bacilli in tuberculous cases through his assistant, Dr. Hemingway.

[7] Old tuberculin.

this line of study. I record it here as a guide to others. I have never seen harm result from the cautious use of tuberculin, as I have sketched it in the diagnostic field. I do not nor does any one that I know of regard the reaction *per se* as diagnostic of the tuberculous nature of any focus, but rather simply that there is a tuberculous focus somewhere in the body though the lesion we may be studying at the time may have little to do with causing the reaction. This is well understood and we meet many cases in practice which illustrate this, and yet there are many physicians who cannot understand this simple fact. The simple presence of tubercle bacilli in an organ without the formation of tubercle tissue will not cause any reaction to tuberculin. This also is not generally understood by the practicing physician.[8]

I cannot close this paper without a reference to a mode of diagnosis which has recently come into clinical use in children with tuberculosis, and that is the X-ray. The X-ray is useful especially in localized bone tuberculosis to fix the location of a focus of disease. It is of value in other forms of tuberculosis, such as meningitis or lung tuberculosis for the demonstration of enlarged mediastinal glands or miliary foci in the lungs. I have recently studied cases of tuberculous meningitis with a view to detecting enlarged bronchial lymph nodes. It was possible to demonstrate the presence of enlarged lymph nodes during life at the root of the lungs, and of miliary foci in the lungs with frequent regularity in cases of meningitis and pulmonary tuberculosis in infants and young children. I cannot say that such Roentgen pictures are of great practical utility until the normal conditions about the root of the lung in infants and children shall have been studied both by the X-ray and autopsy.

[8] Tubercle bacilli are found most frequently in cases with formation of cavities in the lungs and cheesy pneumonia and then are seen in the sputum. The method of examining the sputum described by Holt is here noted but I have not been very successful in carrying it out.

I have found bacilli in the stomach contents and feces especially in advanced pulmonary and peritoneal cases.

Prognosis.

The prognosis of tuberculosis in infancy and early childhood is bad on account of the tendency of the infection at this time to spread and become general. The acute course of fully 75% of the cases has been emphasized in the statistics upon meningitis. The earliest ages at which a tendency of tuberculosis to cure has been observed are the cases of Schlossman and Aronade, 15 and 16 months, respectively. The older the child the better the prognosis. The best prognosis is beyond the age of seven years and I would say that the localized glandular and bone forms have a tendency to heal beyond this age limit.

Prophylaxis.

Much that is disputed ground can for a moment be omitted, and we are face to face with the fact that the greatest danger to the child lies in the vicinity and the surroundings of, the sufferer from tuberculosis. I doubt whether the average physician much less the layman realizes the sacrifice of infant life through the contact of children with tuberculous persons. As I have before intimated, children in the poor quarters of large cities and small ones for that matter are always among the grown-ups. They are the hapless playthings of the old decrepit cougher and the young unsuspecting tuberculous mother. The intimate contact with the mother or father who may be phthisical is at once apparent. It is not uncommon, even in public prints of welfare agitators, to find whole families who are tuberculous. Again vendors of candies and cookies are seen who on the surface are sufferers from tuberculosis. Added to this the universal habit among the poor of expectoration raises the chances of infection among the children. In the face of all this it seems far fetched to ascribe any marked influence in the causation of tuberculosis among children to milk from infected cows.

The future will lie very much in the direction pointed out by Grancher in France; the separation of infants and children from the vicinity of infection, if necessary from parents or vice versa. This is the gigantic work to be done by the city and state boards of health in the future.

THE EFFECT OF THE PREVENTION OF LAKING ON THE CATALYTIC ACTIVITY OF THE BLOOD.

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In the course of a study concerning the influence of feeding potassium iodide on the catalytic activity of the rabbit's blood, some experiments were made to test the effect of this salt when added directly to blood. These experiments were made with the blood of a normal person. The method of determining the catalytic activity of the blood was that used in former experiments.[1] The amount of blood taken was very small, varying from about 0.03 to 0.04 cc. in the entire series of experiments. The different series of experiments are not always comparable with each other because of the varying amounts of blood used. The hydrogen peroxide was neutralized, its strength was approximately three per cent and in each case five cubic centimeters were used.

The arrangement of the experiments was as indicated below. The number of cubic centimeters of liberated oxygen was determined every fifteen seconds for two minutes in duplicate

[1] Strauss: Johns Hopkins Hosp. Bull., 1912, XXIII, 51.

experiments. The figures given are the averages of two well agreeing determinations at the end of one minute.

1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{5}$ KI + H_2O_2.
3. 5.0 water + blood + 5.0 $\frac{m}{5}$ KI + H_2O_2.
4. 5.0 water + 5.0 $\frac{m}{5}$ KI + blood + H_2O_2, not laked.

The number of cubic centimeters of oxygen liberated in sixty seconds was:

1	2	3	4
39.0	5.5	47.5	18.6

Subtracting the amount of oxygen liberated by the potassium iodide solution alone we have:

1.	3	4
39.0	42.0	13.1

It is seen that the potassium iodide solution itself liberates a certain amount of oxygen.[2] When this solution is added to blood which has been taken up in water first, more oxygen is liberated than by the blood alone. But when the blood is added last to a mixture of the potassium iodide solution and water, a very marked diminution of the liberated oxygen takes place. Under this condition the blood is not laked.

In the experiment with addition of the potassium iodide solution to the laked blood the amount of oxygen liberated exceeded somewhat the sum of oxygen liberated by the blood and by the potassium iodide itself. But in other experiments, a simple summation of the effect of blood and of potassium iodide was noted. The experiments were repeated with potassium iodide solutions of different concentrations, always with the result that this marked inhibition did not occur when the blood was laked. On the addition, however, of more concentrated solutions of potassium iodide, as, for instance, a $\frac{m}{25}$ solution, it was noted that after subtracting the oxygen liberated by the iodide solution itself a smaller amount of oxygen was obtained even when the blood was previously laked. Here the known influence of salt solutions on the catalytic activity of the blood becomes manifest, as it did in a number of experiments with solutions of sodium chloride.

For the purpose of this paper it is not necessary to record the results of all experiments with salt solutions of different concentrations. It will suffice to show that the prevention of the laking of the blood depresses its catalytic activity.

In the following tables the results of experiments are given where the blood was not laked, comparing the values with those obtained with blood laked in water without the addition of salt. In the case of the potassium iodide experiments the oxygen liberated by the iodide solution itself is subtracted.

[2] Concerning the mechanism of this reaction see Péchard: Compt. rend. Acad. d. sc., 1900, CXXX, 1705.

A. 1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{5}$ KI + blood + H_2O_2, not laked.
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2, not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2, not laked.

1	2	3	4
39.0	13.1	11.2	12.6

B. 1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{5}$ KI + blood + H_2O_2, not laked.
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2, not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2, not laked.
5. 5.0 water + 5.0 $\frac{m}{25}$ Na citrate + blood + H_2O_2, not laked.

1	2	3	4	5
27.0	8.9	8.2	8.2	7.8

C. 1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2, not laked.
3. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2, not laked.
4. 5.0 water + 5.0 $\frac{m}{25}$ Na citrate + blood + H_2O_2, not laked.

1	2	3	4
25.6	8.0	8.4	8.6

It is evident that the prevention of the laking of the blood reduces its catalytic activity and in this particular case very considerably. The fact that in these experiments the figures obtained are rather constant is very remarkable. For instance the number of cubic centimeters liberated on the addition of $\frac{m}{2}$ or $\frac{m}{5}$ NaCl shows only negligible variations, while the addition of the more concentrated salt solutions to the laked blood causes a very marked depression of its catalytic activity. For instance, taking examples from the series of experiments just referred to:

B. 1. 10.0 water + blood + H_2O_2 } laked.
2. 5.0 water + blood + 5.0 $\frac{m}{2}$ NaCl + H_2O_2 } laked.
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2 } not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2 } not laked.

C. 1. 10.0 water + blood + H_2O_2 } laked.
2. 5.0 water + blood + 5.0 $\frac{m}{2}$ NaCl + H_2O_2 } laked.
3. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2 } not laked.
4. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2 } not laked.

	1	2	3	4
B.	27.0	15.8	8.2	8.2
C.	25.6	14.0	8.0	8.4

The experiments reported thus far were made with the blood of the same individual. In the following experiments the blood of different healthy individuals was used. These experiments are comparable with each other but not with those previously given, because the amount of blood exceeded that used before. The arrangement of the experiments was the following:

1. 10.0 water + blood + H_2O_2.
2. 5.0 water + 5.0 $\frac{m}{2}$ NaCl + blood + H_2O_2 } not laked.
3. 5.0 water + 5.0 $\frac{m}{5}$ NaCl + blood + H_2O_2 } not laked.

The Roman figures designate the different individuals.

	I	II	III	IV
1.	44.2	45.5	37.2	20.5
2.	15.4	15.5	12.9	11.9
3.	15.5	15.6	14.7	12.9

With exception of No. IV the ratio of the catalytic activity of the unlaked blood to that of the laked blood is approximately 1 : 3.

The blood of No. I was used for a series of experiments, in which the concentration of the salt solution was gradually diminished. The strength of a $\frac{m}{5}$ NaCl solution is approximately 1.2 per cent.

	Before addition of H_2O_2.	No. of cc. O_2 liberated in 1 minute.
10.0 1.00% NaCl + blood + H_2O_2	not laked	15.8
10.0 0.66% NaCl + blood + H_2O_2	not laked	16.4
10.0 0.60% NaCl + blood + H_2O_2	not laked	21.7
10.0 0.50% NaCl + blood + H_2O_2	laked.	43.1

There is a marked difference in the catalytic activity with the diminution of the salt concentration from 0.66 to 0.6%, although in both instances there was no apparent difference before the addition of the hydrogen peroxide, the blood not being laked. It is not unlikely that the addition of the five cubic centimeters hydrogen peroxide dilutes the salt solution in the latter case sufficiently to permit a slight laking.

The following experiments made with the blood of another individual support this view:

1. 10.0 water + blood + 5.0 H_2O_2.
2. 10.0 water + blood + 10.0 H_2O_2.
3. 10.0 1% NaCl + 5.0 H_2O_2.
4. 10.0 1% NaCl + 10.0 H_2O_2. } not laked before the addition of H_2O_2.

1	2	3	4
32.0	27.4	9.7	13.6

In Case No. 3, the concentration of the salt solution was reduced to 0.66% by the addition of the hydrogen peroxide, in Case No. 4, to 0.5%. It was found that this salt concentration was not sufficient to insure a complete laking of the blood. In Case No. 2, it is seen that the addition of larger amounts of hydrogen peroxide depresses the catalytic activity to a certain extent. In the following case the same results were obtained. The blood came from a different individual and the strength of the sodium chloride solution was 1.2%.

1	2	3	4
43.7	38.4	16.2	20.0

Here also it is to be noted that this blood did not lake completely with a concentration of sodium chloride of 0.6%.

In spite of the depressing influence of larger amounts of hydrogen peroxide the addition of 10 cc. instead of 5 cc. hydrogen peroxide increased the catalytic activity of the blood unlaked before the addition of the peroxide. This fact is most readily explained by the diminution of the salt concentration.

Therefore in studying the effect of the prevention of laking the blood on its catalytic activity the salt concentration must be such that the addition of the hydrogen peroxide does not reduce it to a hypotonic level.

In order to show the influence of the prevention of the laking of the blood in a different manner a few experiments were made where the blood otherwise unlaked in a $\frac{m}{10}$ sodium chloride solution was laked by the aid of ether.

It was found that the blood could be laked by adding ether to the solution of sodium chloride. The usual amount of blood was added to 5 cc. $\frac{m}{5}$ NaCl. On addition of 0.8 cc. ether the blood remained unlaked, but on adding 4.2 cc. water and shaking, laking took place. The arrangement of the experiments therefore was this:

1. 10.0 water + blood + 5.0 H_2O_2.
2. 5.0 $\frac{m}{5}$ NaCl + blood + 5.0 water + 5.0 H_2O_2, not laked.
3. 9.2 water + blood + 0.8 ether + 5.0 H_2O_2.
4. 5.0 $\frac{m}{5}$ NaCl + blood + 0.8 ether + 4.2 water + 5.0 H_2O_2, laked.
5. 5.0 $\frac{m}{5}$ NaCl + blood + 0.5 ether + 4.5 water + 5.0 H_2O_2, } not laked.

1	2	3	4	5
43.7	16.2	47.9	36.4	16.4

The figure given for experiment No. 4 is an average of four rather widely differing determinations, the single determinations giving 32.4, 34.2, 36.4 and 42.4 cc. oxygen. It is possible that the conditions of the experiment are such as to render a uniform laking less reliable. Nevertheless the results are sufficiently striking to show the discrepancy between the catalytic activity of laked and unlaked blood in salt solutions of the same concentration. The increase of the catalytic activity in No. 3, where ether was added to laked blood is not due to any catalytic activity of the ether employed, since a control with this ether alone did not liberate any oxygen. Neither is it likely that the hydrogen peroxide usually found in ether after standing can be responsible for this increase. It is to be noted that in No. 5, where the amount of ether added was insufficient to lake the blood, the catalytic activity was the same as in No. 2, where no ether had been added.

That the activity of No. 4 did not reach that of No. 3, in spite of the laking of the blood, agrees with other observations

where the catalytic activity of laked blood in a $\frac{m}{10}$ NaCl solution was determined. Here the blood was laked by first adding 5 cc. water and then 5 cc. $\frac{m}{5}$ NaCl. As a rule the catalytic activity of the blood under these conditions fell below that of blood laked in water without addition of salt. With the increase of the salt concentration to $\frac{m}{4}$ this inhibiting effect of the salt became much more pronounced as indicated in the foregoing.

The result of the experiments shows that the prevention of the laking of the blood depressed its catalytic activity. This depressing effect is not surprising, since the investigations of Bergengruen [3] have demonstrated that the power of the blood to decompose hydrogen peroxide resides chiefly in the body of the red blood corpuscles. An experiment with rabbit's blood showed us that the red blood corpuscles yield their catalase to distilled water, while the stromata of the corpuscles after extraction with water are practically inactive.

[3] Bergengruen: Ueber die Wechselwirkung zwischen Wasserstoffsuperoxyd und verschiedenen Protoplasmaformen. Inaugural Dissertation, Dorpat, 1888.

It is remarkable in our experiments that the salt solution of different concentrations depressed the catalytic activity to a rather constant level, provided the concentrations were sufficient to prevent laking. So the catalytic activity of a given blood was not depressed any further, at least not to a marked extent, when the determinations were carried out with a $\frac{m}{4}$ instead of with a $\frac{m}{10}$ NaCl solution; and this in spite of the fact that a $\frac{m}{4}$ solution depressed the catalytic activity of the laked blood very considerably more than a $\frac{m}{10}$ solution.

The possibility was considered whether the comparison of the catalytic activity of the laked and unlaked blood might be able to give us some information concerning the distribution of catalase in the blood, permitting a distinction between catalase contained in the red blood corpuscles and catalase occurring free in the plasma. It is more probable, however, that the explanation of our results lies in another direction, which at present cannot be stated definitely.

Conclusion.

The prevention of the laking of the blood depresses its catalytic activity.

PIN WORM APPENDICITIS.

By Grover C. Ney, M. D.,
Medical Superintendent, Hebrew Hospital, Baltimore.

The occurrence of the oxyuris vermicularis within the appendix is comparatively a common occurrence, but recognized cases of appendicitis caused by this worm are very uncommon, and we therefore wish to report the following two cases which were operated upon at the Hebrew Hospital:

Case 1.—E. M., age 21 yrs., female, married. Admitted to the hospital on January 2, 1911, complaining of pain in her right side, localized at McBurney's point.

Family history: Negative.

Past history: Negative, except for the fact that patient has had some indigestion and is somewhat constipated. There is no history of a previous attack of pain in the region of the appendix.

Present illness: Patient began to have severe pains in her abdomen on December 28, 1910, associated with vomiting; these pains gradually became more severe and paroxysmal in character. Purgatives were administered but failed to relieve the suffering. On the date of admission the pains were so severe that the patient was compelled to have a sedative.

Physical examination: Abdomen negative except that extreme tenderness and some rigidity over the right iliac region are noted. A vaginal examination is negative except for the tenderness elicited on the right side; and a rectal examination is also negative. Urine negative. Temperature 98.4° F., pulse 105, respiration 25. The leucocyte count is 5000; and a differential count shows:

Polymorphonuclears	64
Small mononuclears	30
Large mononuclears	3.5
Transitionals	1.5
Eosinophiles	1

The stools show a considerable quantity of mucus and an occasional Trichomonas hominis. No pin worms were found. In spite of the various negative symptoms an immediate operation was decided upon.

Operation: The abdomen was opened by a right rectus incision and the appendix was found behind the cæcum, bound down by a small adhesion, which was liberated; the appendix was removed, and the stump invaginated. On examination the appendix looked fairly normal, except for a few markedly dilated blood-vessels. It was opened and five pin worms crawled out.

Pathological report: On macroscopical examination the appendix showed some adhesions but no other signs of inflammation. On microscopical examination there were evidences of a catarrhal inflammation of the mucosa, but the other coats were not involved. No eggs of the oxyuris were found upon the mucosa. The worms were active only for a few minutes after the appendix was opened and then died; all were females and filled with ova. Patient made an uninterrupted recovery and left the hospital on January 20, 1911, cured.

Case 2.—F. P., age 17 yrs., female, single. Admitted to the hospital on April 15, 1911, complaining of pain in her right side.

Family history: Negative.

Past history: Has had measles, whooping cough and influenza. Bowels very constipated, appetite good. Has been troubled with indigestion for some time. Has lost some weight in the last year. Gives no history of previous attacks of pain in her right side.

Present illness: About 5 a. m. on the 13th, the patient was seized with severe abdominal pain which finally localized itself on the right side. It continued and grew worse, being extremely severe in the evening. She then had a chill and vomited. On the fol-

lowing day she took calomel, but the pains continued and she finally decided to enter the hospital on the 15th.

Physical examination: Patient's whole appearance indicates that she is suffering a great deal. The examination is negative except for the abdomen, which is extremely tender to pressure over the right lower quadrant, and there is a slight rigidity of the muscles. The vaginal and rectal examinations are negative; the urine is negative. Temperature 99.2° F., pulse 92, respiration 20. The leucocyte count is 19,800.

Operation: Abdomen opened by McBurney incision. There were about 3 ozs. of clear fluid in the Douglas cul-de-sac. The appendix was easily located; there were no adhesions, no concretions and no kinks felt. It was removed and the stump invaginated. The appendix looked fairly normal, but on opening it two pin worms crawled out.

Pathological report: No signs of inflammation made out on macroscopic examination. On microscopic examination the inner layer of the appendix showed signs of catarrhal inflammation. The worms were females and filled with ova; no eggs were found upon the mucosa.

Patient made an uninterrupted recovery and left the hospital on June 8, 1911, cured.

Oxyuris vermicularis is the most common of intestinal parasites. Its ova are probably carried into the body by means of water or vegetables; they are elliptical, measuring from 59 to 72 by 40 to 50 microns, and have an envelope which is absorbed by the digestive juices, when the embryo is liberated within the small bowel. They occupy the intestinal tract from the jejunum to the rectum. These worms were formerly called "seat" worms, from the old idea that they especially inhabited the rectum, but this idea is erroneous. It is true that the females migrate to the rectum to lay their eggs; they slowly wriggle down the mucosa of the bowel to the anal margin, where the eggs are deposited. These worms have been demonstrated by O. Wagener to lie within the deeper layers of the bowel, and Osler has reported cases in which the worms have migrated to the Douglas cul-de-sac. The worms are small, rounded, and tapering at both extremities. Their ends are sharp and penetrating, by means of which they burrow their way into or through the various layers of the intestine. The female worm is much larger than the male worm, being 8 to 12 mm. in length, while the male is only 3 to 4 mm.

As early as 1534 Fabricius ab Aquapendente found a pin worm in the appendix, and Santorini in 1764 confirmed the above fact, and thought the chief function of the appendix was to serve as a nest for the round worm where it might be harbored and prevented from escaping into the general intestinal tract. As the cæcum is the common habitat of the pin worm, they readily crawl into the appendix to lay their eggs. It is possible that in certain cases they cannot escape, but the fact, however, that usually they easily escape does not indicate that they may not have been the prime cause of an attack of appendicitis. By means of their sharp ends they can easily burrow a hole into the mucous membrane; thus they produce a suitable entrance for the bacterial flora of the intestine and set up an inflammation within the non-resistant tissues of the appendix. In this manner a large number of cases of ordinary appendicitis in which worms have not been found could have been produced by the parasites, which had done their damage and then finally departed. If the worm should die within the appendix, the intestinal flora of bacteria acting upon the putrifying worm could also give rise to symptoms similar to the cases of appendicitis in which the lumen of the appendix contains nothing but a small quantity of fecal matter and no signs of inflammation.

There are three classes of cases of pin worm involvement of the appendix. Firstly, pin worms are found in the appendix without symptoms, especially in children. Secondly, there are cases where the worms are found in the appendix giving rise to acute appendicitis with no macroscopical evidence of inflammation, but on microscopical examination small areas of inflammation are found upon the mucosa. Thirdly, the cases with all the clinical symptoms of appendicitis, where the appendix shows macroscopical as well as microscopical areas of inflammation, and even gangrene or peritonitis may be present.

Symptoms: The symptoms of appendicitis due to pin worms vary somewhat from the symptoms of ordinary appendicitis. In our cases we were impressed with two—the extreme hyperæsthesia during the attack and the marked paroxysmal character of the pain. The attacks were agonizing, the patients cried out on the least pressure over McBurney's point. These two symptoms were entirely out of proportion to the degree of inflammation. In both cases we were surprised on opening the abdomen to find the appendices looking macroscopically almost normal. In our cases the attacks were the first attacks of appendicitis, but there are a number of cases reported in which the patients had as many as eight attacks before they were operated upon. The paroxysms last from two to forty-eight hours.

The character of these attacks may be accounted for as follows: these small worms bury their sharp ends into the appendiceal mucosa, which is followed by a peristaltic contraction of the appendix in its endeavor to expel the parasite, thus causing the agonizing colic.

The temperature and pulse in these cases have no particular bearing upon the diagnosis.

The leucocyte count varies and is of no diagnostic significance. The differential count is of no particular importance and the eosinophiles may or may not be increased.

The symptoms bear no relation to the number of worms; which may vary from one to one hundred, those with one or two causing as severe symptoms as those with a larger number. It is true that a large number of worms could lie in a conglomerate mass in the cæcal orifice and obstruct the appendix. This indeed would be an excellent environment to give rise to inflammation and suppuration.

Treatment: The treatment of all cases of pin worm appendicitis is appendectomy, no matter how mild the case. In looking over the literature we find that a large number of the patients have had recurrent attacks of appendicitis, colicky

in character, and some of these have had to be operated upon as emergency cases. Both gangrene and peritonitis have been found. This is probably due to the fact that in the primary attack only small areas of the mucosa are involved and after a number of such involvements the areas of inflammation increase until gangrene results.

In the last hundred cases of appendicitis in the Hebrew Hospital a careful examination of every appendix removed has revealed three cases of pin worms within the appendix.

In conclusion I wish to thank Dr. Randolph Winslow and Dr. St. Clair Spruill for the privilege of both operating upon and reporting these cases which occurred in their services.

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NOTES ON NEW BOOKS.

International Clinics. Vol. IV. Twenty-first Series. (*Philadelphia and London: J. B. Lippincott Company, 1911.*)

The scope of these "Clinics" is gradually enlarging and we are glad to note in this volume two papers on the Economics of Medicine, an important subject to which the majority of the profession has given but little attention. There are other good articles on Treatment, Diagnosis, Medicine, Surgery, Otology, Pædiatrics, Opthalmology, Legal Medicine, the History of Medicine, and Geriatrics—a word quite unfamiliar to most readers, signifying the treatment of diseases of old age. The "Clinics," with their international character as contributions from European and American physicians, offer much of practical value to the general practitioner.

E. Merck's Annual Report of Recent Advances in Pharmaceutical Chemistry and Therapeutics. 1910. Volume XXIV. Darmstadt, July, 1911. (*New York: Merck & Co.*)

There is much that is of value in these reports, for they are carefully prepared in abstract form from the medical literature of all countries, and those interested in pharmacology and therapeutics will frequently find occasion to refer to them. The contents of this well printed, paper-bound volume are as follows: The Cacodylates and their Therapeutic Uses, Kephir, Preparations and Drugs, Bibliographical Index, Index of Authors, General Index, and Index of Diseases, Symptoms and Indications for Treatment.

Spirochætes: A Review of Recent Work with Some Original Observations. By W. Cecil Bosanquet, M. A., M. D., etc. Illustrated. $2.50. (*Philadelphia and London: W. B. Saunders Co., 1911.*)

The author finding himself in possession of an enormous number of abstracts as a result of the necessity of a careful search through the literature on spirochætæ, thought it advisable to use these abstracts in the preparation of a book which would serve as a collective review on the subject.

He has attempted to locate the spirochætæ in their proper place in the scale of living things and feels inclined to consider them as more closely allied to the bacteria than to the protozoa.

The statements of various writers on the morphology and other characteristics of spirochætæ have been correlated with a view of establishing the features of the genus. In the latter part of the book the separate species have been described in some detail. A very valuable bibliography has been appended.

Containing, as it does, a description of all these various organisms, together with details concerning the best methods to be employed in studying them, the book constitutes a distinct addition to any reference library. It fulfils the object of its author and is an excellent review on the subject. L. G. R.

Hints for the General Practitioner in Rhinology and Laryngology. By Dr. Johann Fein. Translated by J. Bowring Horgan, M. B., etc. Illustrated. (*New York: Rebman Company.*)

In the preface, written by the translator, he apologizes for being instrumental in introducing "yet another small book upon the subjects of rhinology and laryngology." This book, however, is an exception; it is far superior to the average compendium in that it is not merely a collection of abstracts from the various textbooks, but consists almost entirely of the personal observations and experiences of the author.

Most of the common lesions of the nose and throat are mentioned, together with some valuable suggestions concerning the local appearance, the various methods which may be used in making a diagnosis, and the treatment of each condition. The book is well worth reading and is, in many ways, an improvement upon works of a similar kind and size.

Report of the Surgeon-General, U. S. Army. To the Secretary of War, 1911. (*Washington: Government Printing Office, 1911.*)

There are several important points brought out in this report, which it is of interest to note. Perhaps the most striking is the proven value of antityphoid vaccinations, which have now been practiced on a large body of men with brilliant results. This is a means of prevention which seems almost, if not quite, as good as vaccination against smallpox, and it is most necessary that the laity should be taught its value, so that in all our larger cities where typhoid prevails annually, the people should make use of this harmless means of guarding against a serious illness when they are exposed to it.

The prevalence of alcoholism and venereal diseases go hand in hand, and those interested in the welfare of our soldiers should strive hard to secure reforms in our barracks. Existing conditions in army life favor these evils, and the proposed remedy of cutting off the soldier's pay when ill from these diseases does not seem an altogether just one, unless means are taken to make his life more endurable at the army posts. If any such remedy is approved by the authorities it should apply to all men in the army, no matter what their rank.

There is a striking table (p. 81) showing "influence of season, United States (excluding Alaska), year 1910," upon the health of the enlisted men. The prevailing diseases, exclusive of venereal diseases, which brought the soldiers into the hospitals or rendered them temporarily non-effective, were during the months of Janu-

ary to June, inclusive, and October, November and December, tonsillitis and acute bronchitis; from July to October, diarrhœa and enteritis. This would at least seem to indicate the necessity of careful examination of the throats of all recruits as well as enlisted men, and the eradication of diseased tonsils, and also a careful study of the diet of the men during the summer months.

Many other points are well worth commenting upon and careful consideration, but those interested in these medical problems will secure the report for themselves, and a thorough study of it will repay them.

The health of the army, on the whole, is most satisfactory, and the work of the army medical officer deserves the highest praise. There is steady improvement all along the line, and we may well feel proud of the medical service in the United States Army.

BOOKS RECEIVED.

Electricity. Its Medical and Surgical Applications, including Radiotherapy and Phototherapy. By Charles S. Potts, M. D. With a Section on Electrophysics, by Horace Clark Richards, Ph. D., and a Section on X-Rays, by Henry K. Pancoast, M. D. With 356 illustrations and 6 plates. 1911. 8vo. 509 pages. Lea & Febiger, Philadelphia and New York.

A Handbook of Medical Diagnosis. In Four Parts. I. Medical Diagnosis in General. II. The Methods and their Immediate Results. III. Symptoms and Signs. IV. The Clinical Applications. By J. C. Wilson, A. M., M. D. 418 text illustrations and 14 full page plates. Third edition, thoroughly revised. [1911.] 8vo. 1438 pages. J. B. Lippincott Company, Philadelphia and London.

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Tuberculous Diseases of Bones and Joints. Their Pathology, Symptoms and Treatment. By Sir W. Watson Cheyne, Bart., C. B., F. R. S., F. R. C. S., D. Sc., LL. D., etc. 1911. 8vo. 404 pages.

A Manual of Fevers. By Claude Buchanan Ker, M. D. (Ed.), F. R. C. P. (Ed.). 1911. 12°. 314 pages.

Manual of Physiology. By H. Willoughby Lyle, M. D., B. S. (Lond.), F. R. C. S. (Eng.). With one plate and 135 figures in the text. 1911. 12°. 747 pages.

Clinical Diagnosis. A Text-Book of Clinical Microscopy and Clinical Chemistry. By Charles Phillips Emerson, A. B., M. D. Third edition. 1911. 8vo. 724 pages. J. B. Lippincott Company, Philadelphia and New York.

Text-Book of Meat Hygiene. With Special Consideration of Antemortem and Postmortem Inspection of Food-Producing Animals. By Richard Edelmann, Ph. D. Authorized translation revised for America by John R. Mohler, A. M., V. M. D., and Adolph Eichhorn, D. V. S. With 152 illustrations and 5 colored plates. 1911. 8vo. 391 pages. Lea & Febiger, Philadelphia and New York.

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THE EFFECT OF EXTENSIVE RESECTIONS OF THE SMALL INTESTINE.

By Joseph Marshall Flint, M. D.,
Professor of Surgery, Yale University.

(From the Surgical Laboratory of Yale University, and the Continuous Surgical Service of the New Haven Hospital.)

Since the appearance of a preliminary communication[1] on this subject, the completion of more experimental work and the appearance of several important papers in the current literature have made it seem desirable to republish it with the inclusion of several new cases, tending to modify, to a certain extent, the conclusions that had been drawn concerning them.

In these days of aggressive surgery, it is important to know the limits of resection of various organs and tissues and, particularly, to be familiar with the response which the organism makes to the loss of large portions of them by reason of either surgical interference or disease. Response to injury or destruction of organs or tissues, either in whole or in part, may be met by several compensatory processes, of which the regeneration of the lost or injured portion represents the most perfect type of compensatory action. In other instances, a hypertrophic process may result either in the remaining portion of the organ or tissues, or sometimes in its mate in case the structure is bilateral.

In general, we now distinguish two kinds of hypertrophy: functional, when a part becomes enlarged through use; and compensatory, when an organ or a part of it is removed and the remainder, or its mate, hypertrophies in consequence. Naturally, the compensatory hypertrophies may also be viewed as the result of extra work caused by the removal of the organs, or a part of them. Although superficial, this distinction between the two processes is not unhelpful, as, in the compensatory hypertrophy, we are usually dealing with an adaptation to neutralize a pathological condition or to offset the effect of an injury. A further useful morphological differentiation of the hypertrophic process was introduced by Virchow, who speaks of hypertrophy in the sense of an enlargement of the cells, and of hyperplasia as indicating an increase of the number of cells of which the tissue or organ is composed.

Still another type of compensation, which seems to be vicarious in nature, is where one organ may show compensatory action on behalf of another from which it may be, so far as we know, physiologically different. Of this type of compensation we know least, although it will form one of the most interesting chapters in the future development of experimental medicine.

To determine which of these compensatory processes was involved, some eleven years ago, at the suggestion of Dr. F. P. Mall, Dr. R. F. Rand and myself began to study the effects of removing large portions of the small intestine. Our period of collaboration, unfortunately, ended with the completion of the operations, and since that time I have only had sporadic opportunities to finish the study of the preparations which we obtained, and to perform such new experiments as the progress of the work demanded.

[1] Flint. Trans. Conn. State Med. Soc. 1910, 283.

Methods and Materials.

Dogs were selected for experiments, partly because of their well-known resistance to operative procedures, but largely because the finer anatomy of the intestine in the dog has been exhaustively studied by numerous investigators. The dogs were prepared for operation with scrupulous care, and all of the usual aseptic precautions were taken. After a thorough disinfection of the skin, the abdominal cavity was opened. The whole movable portion of the small intestine, that is to say, the combined jejunum and ileum, was then delivered into the wound. In this way, the duodenum and a part of the jejunum was excluded from the operation, owing to their fixation and the anatomical relations, which made it impossible either to resect or to measure them for the purpose of control in determining whether there had been a regeneration in the portion of the intestine left in the body. Accordingly, it was our custom, during the first operations, to mark the upper end of the jejunum by a black stitch and, from this point, the measurements of the intestines were taken. These stitches proved, however, entirely too uncertain and, finally, we had recourse to a subserous injection of lampblack, sterilized in salt solution, which gave an indelible tatoo, forming a permanent and terminal landmark from which the combined jejunum and ileum could be measured. As a preliminary stage of the operation, it was our custom to measure the whole of the small intestine from the tatoo mark on the jejunum to the cæcum. Owing to the great elasticity of the gut, this measurement could not be made absolute; so one of us, the writer, always measured the intestine by applying as nearly as possible the same tension upon the gut, while protecting it from the longitudinal shrinking that follows its exposure to the air, by means of gauze pads soaked in warm salt solution. Although there is always a slight error in the measurements, the method, nevertheless, is relatively accurate, as the determinations were always duplicated and the mean used as the determined length. In two such measurements of the intestine, there was rarely a discrepancy of more than 30 cm., which would place the average error in determining the length of the whole portion of the gut with a free mesentery, at about 15 cm. As the measurements were taken, marks and measurements were made to determine the position of the upper and lower points of the portion to be resected, which gave us an additional landmark in the suture to determine whether there was a lengthening of the segment of the intestine left at operation. The mesenteric vessels were then tied, and a fan-shaped piece of mesentery cut leading to the points of section. After resection of a segment, the continuity of the intestine was re-established by an end-to-end anastomosis. For purposes of control and comparison, the resected portion of the intestine, after the completion of the operation, was stretched to its measured length in the body, opened, washed, and rolled around a glass cylinder in such a way as to keep the mucosa from being injured while the specimen was being fixed and hardened in formalin.

In a later series of experiments, a functional resection of the intestine was accomplished by means of a short-circuiting lateral anastomosis with the invagination of the upper end of the lower segment of the gut. To prevent intussusception, this end was stitched to the abdominal wall. Thus the functionless portion remained in the abdominal cavity, to be compared at autopsy with the measurements taken at operation. Furthermore, an absolute comparison of the short-circuited segment with that retaining its functional activity is possible by means of the distension of both segments simultaneously with an equivalent hydraulic pressure. Dogs Nos. 12, 13 and 14 are examples of this series.

The metabolic disturbances following the resection of the intestine were studied by Drs. Erlanger and Hewlett, to whom were loaned Dogs Nos. 2, 9 and 10, and whose results will be considered in detail later. My colleague, Professor Underhill, determined the metabolic changes in Dogs Nos. 12, 13 and 14, upon which a short-circuiting operation was done. For the morphological changes, I have used all of the microscopic methods which might throw any light upon the changed structure of the intestine. In order to have an absolute method of comparison in studying any modifications that might occur in the mucosa, the Born wax plate reconstruction method was employed. Further details concerning the technique will be given, as they may have a bearing on the interpretation of the results.

Experiments.

The general results of the operations for the purpose of our study may be collected in the following table:

TABLE

Dog No.	Sex	Weight, pounds	Length of ileum and jejunum	Resected	% Removed	Table: Whole length small intestine	Table: % Removed.	Table: Days lived	Result	Remarks—Cause of death
1	F	25	287	55	19					
1*	F	29	222	176	61	348	66	110	Recovery	Killed for observation.
2	M	22	232	80	34					
2*	M	23	175	84	36	301	54	451	Recovery	Killed for observation.
3	F	27	316	132	43	...	..	28	Died	Pneumonia.
4	M	38	291	209	72	...	..	32+	Recovery	Escaped from dog house in good condition.
5	M	14	227	183	80	252	70	9	Died	Ileus from adhesions.
6	F	29	323	295	91	...	..	10	Died	Omental hernia, peritonitis. Infection of abdominal wound.
7	M	20	198	174	87	219	79	9	Died	Omental hernia, peritonitis. Infection of abdominal wound.
8	F	22	339	288	85	...	..	6	Died	Omental hernia, peritonitis. Infection of abdominal wound.
9	F	29	357	298	83	458	65	220	Recovery	Died during metabolism experiments.
10	F	23	289	238	81	334	70	322	Recovery	Killed for observation.
11	M	31	425	364	85	...	..	17	Died	Abscess about suture.
12†	F	..	...	237	..	323	73	213	Recovery	Killed for observation.
13†	F	..	525	350	66	...	..	...	Recovery	Killed for observation.
14†	F	..	412	162	39	...	..	...	Recovery	Killed for observation.

* Second operation.
† Intestine not resected. Segment short-circuited by enteroenterostomy.

It may be well to recall, however, that the measurements are only approximate, as it is impossible to determine absolutely the length of an elastic organ in the body of a living animal. Furthermore, the recorded length is perhaps consid-

erably greater than normal, as the intestine, during the measurement, was put under slight tension to counteract the effect of the action of the longitudinal layer of the *tunica muscularis*.

In all, sixteen operations are recorded, two of them being upon dogs from which a portion of the gut had already been removed. Of the sixteen operations on fourteen dogs, six died from all causes, making a total mortality of 37 per cent. In no case, however, could the reaction of the intestine *per se* be looked upon as the direct or primary cause of death, although it might naturally be considered a contributory factor in reducing the resistance by causing profound metabolic disturbances, as was evidenced by the extreme diarrhœa and loss of weight. From the table and protocols given above, it will be seen that three died from infection resulting from a breaking down of the abdominal wound; one died from ileus in consequence of adhesions about the intestinal suture; one died from pneumonia, and the last from inanition, induced by the metabolism experiments, after living 213 days.

From the general clinical observations[2] on the operated animals, we found that relatively large portions of the small intestine in dogs may be removed without danger to the life of the animal. The maximum is difficult to determine, as the immediate effect of the operation would, no doubt, depend to a great extent on the general condition of the dog at the time the resection was made. But this much can be said: dogs from which about 80 per cent of the combined ileum and jejunum have been removed, or short-circuited (Dogs Nos. 1, 9, 10 and 12) may live indefinitely after the operation. The first effects of the operation give a profuse diarrhœa and loss of weight, from both of which the animal slowly recovers. At the same time, the resection of a smaller amount, *i. e.*, 65 per cent of the entire intestine (Dogs Nos. 9, 12 and 13), may lead, notwithstanding a ravenous appetite and an unlimited diet, to changes which prevent the dog from regaining its former well-nourished condition. In these animals the nutrition may be apparently normal, but they are, nevertheless, so sensitive to diatetic disturbances that a diet or conditions of any severity may introduce a fatal marasmus or enteritis (Dogs Nos. 9, 12 and 13). Young growing animals (Dogs Nos. 3, 8 and 11) apparently do not stand the operation of the removal of large amounts of the intestine as well as older dogs, and those cases (Dogs Nos. 1 and 2) where two operations were performed, that is to say, where the resection was fractional, recovered sooner and with greater ease than where the entire resection was made at one sitting.

Metabolic Experiments.

A number of months after the operations, three dogs, Nos. 2, 9 and 10, were loaned to Drs. Erlanger and Hewlett, who wished to study the effects of shortened intestines upon metabolism. Their results have already appeared in another place, and, from this paper, the following brief summary of their conclusions may be given. In their series, No. 1 corresponds to our No. 2, No. 2 to our No. 10, and No. 3 to our No. 9. Owing to a misunderstanding of our methods of numbering both dogs and operations separately, the corresponding figures are incorrectly given in their paper. When an easily absorbable diet is given, dogs with shortened intestines behave like normal dogs. The fat and nitrogenous content of the fæces may not exceed the normal. Upon increasing the fat in the diet, however, the abbreviation of the intestine shows its influence on the power of absorption. Under these conditions, the percentage of both fat and nitrogenous material in the fæces may reach a fourth of that which is ingested in the diet. Notwithstanding this fact, the animals increased in weight, as relatively a large amount of fat is absorbed. The diminished absorption is simply an index of the effect of resecting large portions of the intestine upon the power of absorption, which may also become evident when the ordinary diet contains many indigestible substances.

Neither in quantity, specific gravity, or nitrogenous content, did the urine of dogs with shortened intestines show any differences from that of normal animals. There was, however, an absolute increase in the quantity of the conjugated sulphates, and a relative increase in the alkaline sulphates, indicating an excess of intestinal putrefaction. In Dog No. 2, from which 54 per cent of the entire small intestine had been removed, there was no marked increase in the quantity of fæces. In Dog No. 10, however, from which 70 per cent had been resected, there was an increase in the amount. In both dogs, the percentage of water in the fæces was equal to or only slightly in excess of that in normal dogs, which is in contrast to the increased percentage in dogs deprived of the large intestine (Harley). The shortening of the intestine has no effect on the absorption of fat when the animal is on a diet poor in fat. As this element of the diet is increased, the fat in the fæces may increase to 25 per cent in a normal dog. This increase, in normal animals, does not markedly accentuate the elimination of nitrogenous material in the fæces. With a shortened intestine there is an increase which may equal an amount double that eliminated by a normal dog, although on a diet poor in fat, there appears to be no great difference between the two.

De Filippi studied the metabolic changes in a dog from which Monari had removed seven-eights of the small intestine, and in which only one-eighth of the combined ileum and jejunum remained. In this instance, he found that the carbohydrates were completely utilized, that the nitrogen loss was not much greater than in normal dogs, while the continued diminished fat absorption (19 per cent of the total amount ingested recovered in the fæces) made a richer diet for the animal necessary.

Of special importance in connection with the investigations of De Filippi, and of Erlanger and Hewlett are the observations and ileum from two dogs. In one instance he removed the jejunal half, while in the other the lower half was resected. Unlike the other investigators, Diliberti-Herbin was able to conduct experiments on his animals from the time of the

[2] Detailed descriptions of the operations and the post-operative behavior of the animals are included in the preliminary report.

operation and found that the nitrogen and fat excretion varied from 33 per cent to 66 per cent, and remained high for a long period. Ultimately, however, the conditions became more normal.

The results of the metabolism experiments on dogs may be tabulated as follows:

Investigators	Animals	Resection	Percentage of diet nitrogen in fæces	Percentage diet fat in fæces	Perc. diet carbohydrate in fæces
De Filippi	Monari's dog.	190 cm.	Slightly increased	19%	None.
Erlanger and Hewlett	Dogs Nos. 2, 9, 10	54%, 65%, 70%	Normal to 25%	Normal to 25%	No obs.
Diliberti-Herbin	His own.....	50%	33% to 66%	33% to 66%	No obs.
Underhill.....	Dog No. 12...	73%	25.9%	27.7%	None.
Underhill.....	Dog No. 13...	66%	13-19 %	9-34%	None.
Underhill.....	Dog No. 14...	39%	13-16 %	10-14%	None.

From these observations, a number of interesting facts may be found which explain the clinical observations made upon our dogs. The resection of large amounts of the intestine, by diminishing the absorbing surface of the gut, disturbs the balance in the nitrogen and fat absorptions, and leads to an excessive excretion of these elements in the fæces, an increase which may reach two-thirds of the quantity ingested. This accounts for the profuse diarrhœa invariably observed after the operation. Owing to the limited surface of absorption of nutritive substances, the animals are, for a time, forced to consume the nitrogen and fats of their own tissues. Gradually, however, a balance is restored and the excessive excretion of these elements diminishes, until, as Erlanger and Hewlett have shown, the animals, with the exception of an increased intestinal putrefaction, may return to practically normal nutritive conditions. That this restoration of the power of absorption is not complete, however, may be shown by the susceptibility of the dogs to either diets containing indigestible substances, or to diets rich in fats, which lead to diarrhœa, and an excessive excretion of both nitrogenous and fatty elements of the foods. Thus the compensatory mechanism is apparently effectual under favorable conditions of diet and life, but the result is by no means as efficient as the power of absorption of a normal intestine.

In contradistinction to the fat and nitrogen metabolism, however, the carbohydrates in the diet appear to be completely utilized after the compensation has been established (De Filippi, Underhill). It would appear that we have in carbohydrates a more easily assimilated food which can be utilized by animals with shortened intestines, even when fats and nitrogen are excreted in a percentage above normal. In his experiments, Underhill quadrupled the amount of an ordinary carbohydrate diet for a dog of this weight, and still obtained no test. During the metabolism experiments the dog had soft stools, and Underhill observed the water content of the fæces varied between 80 and 84 per cent, which is about 5 to 10 per cent above normal. In a second series of observations carried out upon Dogs Nos. 13 and 14, two weeks after the short-circuiting operation, Underhill obtained no test for carbohydrates in the fæces, indicating an ability on the part of the animals to utilize these easily assimilated foods even during the period when the excretion of the fatty and nitrogenous elements of the diet was at its maximum. The practical significance of these observations should not be overlooked, and will be commented upon later.

The increased putrefaction is undoubtedly due, as Erlanger and Hewlett point out, to the fact that the food remains for a longer period, under the altered circumstances, in the large intestine, exposed to the action of the bacteria, for these dogs, after the compensation is established, have only the normal number of stools per day, and may even be constipated (Dog No. 9).

Besides the experiments on the metabolism of dogs with shortened intestines, there have been several cases reported where observations were made upon the modification of the nutritive processes after extensive resections of the human ileum. An account of these cases is of particular interest, not only for the confirmation which they bring to the observations made upon animals, but because they make it probable that the results obtained from animals may be also applied to man.

Sagini carried on metabolic experiments upon a patient of Ruggi's, a boy of eight years, from whom the latter had removed 330 cm. of small intestine in three sittings. His observations extended over two three-day periods. The first series gave a nitrogen excretion of 5.9 per cent, and a fat excretion of 12.1 per cent, results which were practically normal according to this investigator. The second series yielded a nitrogen excretion of 13.2 per cent and a fat excretion of 15.3 per cent. The averages of these two series of estimations were 9.5 per cent for the nitrogen elimination, and 13.7 per cent for the fat excretion. About the same time, Riva-Rocci studied the metabolism of Fantino's patient, who was sixty years of age, and from whom 310 cm. of the combined ileum and jejunum had been removed. The experiments began eighteen days after the operation, and lasted two weeks. The nitrogen loss varied between 24 and 40 per cent, with an average of 29 per cent, while the fat excretion varied between 17.2 and 34.3 per cent, with an average of 23 per cent. These amounts are somewhat in excess of Riva-Rocci's normal, but, notwithstanding, the patient continued to gain in weight and make an uninterrupted recovery. Riva-Rocci, therefore, concludes that the removal of 300 cm. of the small intestine may effect the metabolism, but not to a sufficient extent to complicate recovery or affect materially the health of the patient. Schlatter removed 192 cm. of gangrenous intestine from an Italian who was suffering from a stab wound of the abdomen. In the metabolism experiments, which Platt carried out in this case, the nitrogen excretion was 10.47 per cent, and the fat excretion 13.93 per cent. The patient recovered and gained in weight. His digestion was considerably impaired, however, and special, easily assimilated food was demanded. Moreover, the patient tired easily, and never succeeded in establishing a true metabolic compensation for the lost intestine. Schlatter concludes, therefore, that the digestive processes may be seriously disturbed by the resection of

more than 200 cm. of small intestine in young persons, unless a rich diet can be provided. Later, Schlatter communicated by letter to Albu the fact that his patient had been, after some two years, so improved that he could live in health upon the ordinary frugal diet of his people (Italians). The improvement had been slow, similar to the gradual recovery of the power of absorption by dogs with shortened intestines.

The case of Lexer, from which 200 cm. of small intestine had been resected, was observed by Albu, who studied the metabolism changes following the operation. The diet which he gave his patient contained 17 grams N., 88 grams fat, 328 grams carbohydrates. Of this amount, the patient lost 10.12 per cent of the diet nitrogen, and 10.1 per cent of the fat in the fæces. The indican was normal in the urine and, therefore, there was probably no increase of intestinal putrefaction. From his study of this case of Lexer, Albu concludes that not more than one-third of the small intestine may be removed without danger to the nutrition, even when that third is computed on the relative length of the intestine to body weight.

Miyaki has reported a case in which 225 cm. of the ileum and 13 cm. of the colon was excised for tubercular ulcers and adhesions. Upon this case Onodera and Jano, two months after the operation, carried out studies in metabolism, which showed a nitrogen excretion of 29.8 per cent, fat elimination of 31.7 per cent, and 0.43 per cent of the diet carbohydrates in the fæces. Although the patient had from one to three stools a day, these observers looked upon this as a practically normal excretion. Seven months later, the patient had only one or two formed stools, and had gained 9.5 kilos in weight. In comparing these figures with other cases, however, particularly in reference to the carbohydrate elimination, it should be remembered that the Japanese diet is particularly rich in carbohydrates.

One of the most extensive resections of the human intestine was made by Nigrisoli, who removed 520 cm. of the small intestine for adhesions and stricture. Vitali studied the metabolism on Nigrisoli's case in a series of observations beginning twenty-two days after the operation, and lasting some twenty-three days. During this period the patient gained some 5 kilos, but Vitali observed, notwithstanding, an increase in the excretion of nitrogen and fats to an extent slightly above normal, as well as an increase in intestinal putrefaction as indicated by the excess of the ethereal sulphates in the urine, thus confirming on man the observations of Erlanger and Hewlett on our dogs. Besides Brugsch, whose work will be described later, Vitali was the only investigator who studied the carbohydrate metabolism in human beings. These substances. like the nitrogen and fat, were also excreted in excess of the normal, a fact, it will be observed, which does not correspond to the metabolic studies on animals with shortened intestines, at least after the compensation has been established.

Zeidler operated upon a young man of twenty, with a large scrotal hernia, in which the contents of the sac had become incarcerated, resulting finally in torsion and gangrene of the intestine. Resection of 318 cm. was necessary. The patient made a good recovery, and two months after the operation, Spassokukozkaja studied the nitrogen metabolism, which he declared was normal. In the abstract, no mention is made of any observations upon the fat or carbohydrate metabolism.

A carefully worked up case of resection of 475 cm. of the small intestine is reported by Axhausen, who removed this large segment of the ileum for vovulus and gangrene in a young woman aged eighteen. This operator measured the remaining portion of the intestine by handspans and estimated about 125 cm. of the jejunum and ileum was left, after the gangrenous portion had been removed. In this case the metabolic changes were studied by Brugsch. As the patient had a tubercular process in each apex, the appetite was poor, and only a moderate amount of food was taken. The diarrhœa was not marked, as there were only two or three soft stools a day, fatty in character and of silver gray color. Microscopically, they showed many fatty acid and soap crystals, undigested muscle fibres, with nuclei and cross striations in good condition. The metabolic observations began sixteen days after operation and showed 36.5 per cent of the diet fat in fæces, of which 25.2 per cent consisted of neutral fats, 24.8 per cent of fatty acids, and 40 per cent of soaps. Of the nitrogen content of the food, 34.2 per cent appeared in the fæces, while the carbohydrates were completely utilized, an interesting confirmation of Professor Underhill's observations on Dogs Nos. 12, 13 and 14. Furthermore, an increase in the amount of ferments in the stools over the normal was observed.

The patient maintained her weight for about three months, but gradually failed, and died of tuberculosis six months after the operation. As Axhausen remarks, her impaired intestinal absorption was probably not without effect on the course of the tubercular process.

Another case of extensive resection of the small intestine is reported by Storp, who excised 510 cm. of the ileum for a sarcoma of the mesentery. There was a slight diarrhœa after the operation, the patient having two or three soft stools a day. Although this was controlled by astringents, it showed a tendency to recur. Notwithstanding, the patient gained in weight, although a microscopic examination of the stools showed more fat and fatty acid crystals than normal. Otherwise, no study was made of the balance between ingestion and elimination in this case. A short time later multiple metastases were found in various parts of the body, and the patient was discharged without further treatment, owing to the hopelessness of the condition.

Denk reported the two cases of extensive resection of the ileum operated on by Brenner of Linz. The first was a case of intussusception from a polyp, for which 250 cm. was removed. The patient showed no digestive disturbances. The second case is the largest reported resection in the literature, where Brenner removed 540 cm. of the ileum in a woman aged sixty-one, for gangrene, due to torsion of the intestine in a large femoral hernia. The patient made an excellent recovery, and showed but little disturbance of her metabolism. She had about five fluid stools a day, which were bad-smelling, and contained much undigested food. Later, conditions improved,

and Denk made a test of the functional efficiency of the intestine by Schmidt's method, which indicated a normal digestion. About one and one-half years after the operation, Denk repeated the test. At this time she had from three to four soft or fluid stools a day, the latter condition occurring particularly after taking much coffee or milk. Although there was a diminished fat absorption, the patient maintained her weight and was able to do her housework without fatigue. Otherwise, the metabolism was perfectly normal.

A subsequent report on this case made by Denk recently shows the importance of a guarded prognosis even in apparently successful cases of extensive resection of the small intestine. A year after the last report was published, or 2½ years after the operation, the patient died of marasmus. At the time of operation, the patient weighed 48 kilos, and just before death, 26½ kilos. There was a general atrophy of all the organs, particularly of the omentum, confirming in main, the conditions found in some of our experimental animals (Fig. 1). No compensatory hypertrophy of the intestine was found in the case.

My own second case, which is reported in detail later in this paper, was studied metabolically by Underhill, who found that the infant of 11 months of age, showed during the period of severe diarrhœa 10 days after the operation, an increase in the fat excretion and an incomplete utilization of the carbohydrates, as a test for lactose was obtained. In the second series of experiments, made five weeks after the operation, after compensation was established, the fat excretion had dropped from 20 per cent to 9 per cent, and no test for lactose was present, although carbohydrates were excreted to the extent of 5 per cent, due to the presence of an indigestible cereal in the food.

The results of the metabolic studies on the human cases may be tabulated as follows:

Investigator	Case	Resection	Per cent of diet N. in fæces	Per cent of diet fat in fæces	Per cent of diet carbohydrate in fæces	Intestinal putrefaction
Underhill	Flint's	100	15	21	1	No obs.
Underhill*	Flint's	100	16	8	4	No obs.
Plaut	Schlatter's.	192	10.47	13.91	No obs.	No obs.
Albu	Lexer's	200	10.12	10.1	No obs.	Not increased
Onodera & Jano	Miyaki's	238.5	29.8	31.7	0.43	No obs.
Riva-Rocci	Fantino's	310	29.0	23.0	No obs.	No obs.
Zusch	Barth's	316	13.7–21.3	18.1–38.5	0.54–0.61	No obs.
Spassokukozkaja	Zeidler's	318	Normal	No obs.	No obs.	No obs.
Sagini	Ruggi's	330	9.5	13.7	No obs.	No obs.
Brugsch	Axhausen's	475	34.2	36.5	0	No obs.
Vitali	Nigrosoli's.	520	Incr'sed	Incr'sed	Incr'sed	Incr'sed
Denk	Brenner's	540	Normal	Incr'sed	Trace	Not increased

* Second period.

An inspection of this table containing the observations on those cases of extensive resection of the small intestine in man where the metabolic changes were studied, confirms, in general, the findings upon the metabolic processes in dogs with shortened intestines. There is no constant ratio between the length of the resected portion of the ileum and the degree to which the absorption of nitrogenous and fatty substances is diminished. The difficulty in harmonizing these results is due, no doubt, to the differences in the diets on which the patients were tested, and to a number of unknown factors, such as the exact length of intestine left at operation, or, in other words, the variability of the intestine, difficulties of measurements, resistance and condition of the patient, not to speak of the known variations of age, pathological conditions, etc. In general, however, the results of these observations are in accord with those upon animals. Moreover, the subsequent history of Schlatter's case, as told in his letter to Albu, indicates that the same gradual improvement observed in dogs also takes place in man. As in the observations in dogs, the increased intestinal putrefaction is undoubtedly due to the food remaining for a longer period than normal in the large intestine.

TABLE OF CASES OF RESECTION OF SMALL INTESTINE EXCEEDING 200 CM.

No.	Operator and publication	Amount resected cm.	Result	Metabolic disturbances	Remarks
1	Flint: Johns Hopkins Hosp. Bull., 1912, xxiii, 133.	Ileum, 100 Colon, 18	Recovery	Severe	Intussusception and gangrene. Infant 11 months old.
2	Lexer Berl. klin. Wchnschr., 1900, xxxvii, 4.	200	Recovery	Moderate	Fibroma of mesentery.
3	Peterson: Ref. Ruschhaupt, Inaug. Diss., Bonn, 1901.	202	Recovery	None	Prolapse of intestine. Stab wound of abdomen.
4	Flint: Johns Hopkins Hosp. Bull., 1912, xxiii, 135.	Ileum, 204 Colon, 55	Death	Violent	Colloid carcinoma of transverse colon and intestinal adhesions.
5	Kocherlé: Gaz. hebd. de méd., 1881, 2. s., xviii, 55.	205	Recovery	None	Stricture.
6	Miyake: Arch. f. klin. Chir., 1910, xciii, 768.	206	Death	....	Adhesions to ovarian tumor. Death. Peritonitis.
7	Enderlen: Ref. Lauenstein, Deutsche Ztschr. f. Chir., 1909, c, 169.	207	Recovery	....	Strangulated hernia.
8	Kocher: Ref. Trzebicky, from letter.	208	Recovery	Slight	Rupture of intestine.
9	Dreesman: Berl. klin. Wchnschr., 1899, xxxvi, 337.	215	Recovery	Moderate	Gangrene, incarcerated hernia.
10	Mikulicz: Rothe, Beiträge z. klin. Chir., 1902, xxxiii, 140.	215	Recovery	None	Gangrene. Hernia.
11	Karlow: Hygiea, 1903, f. iii, pt. 2, 460.	215	Recovery	None	Gangrene, omental bands.
12	Axhausen: *vide inf.*	215	Recovery	....	Tubercular stricture of intestine.
13	Dekonski: Ref. Istomin, Russ. med. Rundschau, 1910, viii, 329.	220	Recovery	....	....
14	Thon: Deutsche med. Wchnschr., 1909, xxxv, 742.	220	Recovery	....	Ileus.
15	Kouwer: Nederl. Tijdschr. v. Geneesk., Amst., 1898, 2, R., xxxiv, d. 2, 887.	224	Recovery	None	Gangrene, hernia.
16	Miyake: Loc. cit.	Ileum, 225.5 Colon, 13	Recovery	Slight	Tubercular ulcers and adhesions. Two to three soft stools *per diem.*
17	Monprofit: Rev. de Chir., 1899, xx, 579.	Ileum, 230 Colon, 80	Recovery	Slight	Adhesions, hernia.
18	Shepard Centralbl. f. Chir., 1898, xxv, 397.	237	Recovery	Slight	Tumor mesentery.
19	Kukula: Arch. f. klin. Chir., lx, 877.	237	Recovery	None	Tumor mesentery. Recurrence 1½ yrs. later. Death.
20	Harris: Med. Rec., N. Y., 1902, lxii, 563.	239	Recovery	Slight	Gangrene, hernia.
21	Hayes: Blayney, Brit. M. J., 1901, i, 399.	248	Recovery	Slight	Rupture of mesentery.
22	Brenner: Denk. Wien. klin. Wchnschr., 1907, xx, 1649.	250	Recovery	None	Intussusception from polyp.
23	Enochin: Ref. Istomin (see Dekonski).	250	Recovery	....	.....
24	Peck: Ref. Harris.	251	Recovery	....	Rupture of uterus.
25	Lauwers: J. d. Chir., et Ann. Soc. belge de Chir., 1901–2, i, 739.	265	Recovery	....	Gangrene hernia.
26	Park: Arch. interuat. de Chir., 1904, i, Fasc. 1.	265	Recovery	....	Gangrene following appendicitis.

TABLE OF CASES OF RESECTION OF SMALL INTESTINE EXCEEDING 200 CM.—*Continued.*

No.	Operator and publication	Amount resected cm.	Result	Metabolic disturbances	Remarks
27	Pokotilo: Chirurgia, 1909, xxv, 169.	270	Recovery	....	Strangulated hernia.
28	Mitchell: Ref. Kelly-Noble Abdominal Surg'y. Phila., 1908, p. 442.	274	Death	....	Thrombosis of mesenteric artery.
29	Payr: Arch. f. klin. Chir., 1902, lxvii, 181.	275	Recovery	None	Gangrene.
30	Kopfstein: Revue d. Böhm. Med., 1909. Ref. Wien. med. Bl., 1910.	275	Recovery	Slight	Tubercular stricture of intestine.
31	Mayndl: Ref. Kukula.	284	Death	Inanition	Carcinoma of cæcum. Death in 21 days.
32	Childe: Brit. M. J., 1907, ii, 891. Practitioner, 1909, lxxxii, 364.	289	Death	Inanition	Gangrene, hernia. Died 7 months after operation, from inanition.
33	Lorenz: Wien. klin. Wchnschr., 1906, xix, 610.	292	Recovery	....	.....
34	Göbell: Deutsche Ztschr. f. Chir., 1905, lxxvii, 608.	300	Recovery	Slight	Mesenteric hernia and volvulus.
35	Friedrich: Med. Klin., 1904-5, i, 25.	300	Recovery	....	Septic peritonitis, short-circuiting without resection.
36	Fantino: Riforma med., 1902, xviii, pt 4, 736, 748, 758.	300	Death	Inanition	Adhesions to fibroma uteri. Death one month later.
37	Fantino: Gazz. med. di Torino, 1896, xlvii, 181.	310	Recovery	Moderate	Gangrene, volvulus.
38	Ghodini: Clin. Chir., Milano, 1905, xiii, 278.	315	Recovery	....	Strangulated hernia. Death in 3½ mos. Marasmus.
39	Barth: Deutsche med. Wchnschr., 1909, xxxv, 509.	316	Recovery	Slight	Ovarian tumor, fecal fistula, short-circuiting, later resection of short-circuited loop.
40	Fischer: Ref. Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1906, ix, 70.	316	Recovery	....	Incarcerated hernia.
41	Zeidler: Spassokukozkaja, Russk. Vrack. 1906. Ref. Centralbl. f. Chir., 1906.	318	Recovery	....	Hernia.
42	Whitall: Ann. Surg., 1911, liv, 669.	320	Recovery	None	Abortion. Perforation of uterus.
43	Morton: Ref. Kelly Noble Abdominal Surg'y, Phila., 1908, p. 442.	322	Recovery	....	Myxosarcoma of mesentery.
44	Ruggi: Centralbl. f. Chir., 1896, xxiii, 365.	330	Recovery	....	Strangulation and adhesion. Three operations.
45	Staehlin: Ann. Surg., 1907, 45, 49.	335	Recovery	Slight	Strangulated hernia. Recovered perfectly.
46	von Eiselsberg: Ref. Park.	350	Death	Inanition	Lived 25 days.
47	Baracz: Arch. f. klin. Chir., 1907, lxxxiii, 478.	350	Death	....	Strangulated hernia gangrene; lived 2 days.
48	Nicola: Clin. chir., 1910.	350	Recovery	....	Incarcerated umbilical hernia.
49	Werelius: J. Am. M. Ass. 1907, xlviii, 945.	365	Recovery	Slight	Abortion, rupture of uterus.
50	Obalinski: Arch. f. klin. Chir., 1894, xlviii, 16.	Ileum, Cæcum, 365	Death	....	Gangrene, hernia; died in 22 hours.
51	Mitchell: Brit. M. J., 1902, ii, 975.	366	Recovery	....	.....
52	Pauchet: Ref. Gazz. d. hôp., 1905, 1667.	400	Recovery	Violent	Gangrene, hernia.
53	Friedrich: Med. Klin. 1904-05, i, 25.	400	Recovery	....	Functional short circuit.
54	Axhausen: Mitth. a. d. Grenzgeb. d. Med. u. Chir., 1909, xxi, 55.	475	Recovery	Moderate	Volvulus, death 6 months later, tuberculosis.
55	Stolz: Deutsche med. Wchnschr., 1909 xxxv, 744.	475	Recovery	Slight	Fatigue after exertion.
56	Storp: Deutsche Ztschr. f. Chir., 1907, lxxxvii, 313.	510	Recovery	Moderate	Sarcoma of mesentery; recurrence, death.
57	Nigrisoli: Jahresbe. f. Chir., 1902, viii, 754.	520	Recovery	Moderate	Obstruction from adhesions.
58	Ghedini: Loc. cit.	524	Recovery	Slight	Strangulated hernia. Short-circuited.
59	Brenner: Denk, Wien. klin. Wchnschr., 1907, xx, 1649.	540	Death	Slight inanition	Gangrene, hernia Died of marasmus 2½ years after operation.

In addition to the cases on which metabolism experiments were conducted, there are many others in the literature where large amounts of the small intestine have been resected. Some of these have shown digestive disturbances and others not. As I have succeeded in finding fifty-eight instances, including the cases reported in this paper, where 200 cm., or more of the intestine have been removed, a list of the cases is given above, together with the chief points of interest in the history.

In consideration of this series of cases, several facts should be borne in mind. In the first place, in the measurement of an extremely elastic organ like the intestine, there has been no standard to guide the investigators who have reported the various cases. Great errors are thus unconsciously liable to exist. Furthermore, there may be extreme differences in measurement, due to the viability of the gut. Living intestine, exposed to the air, will, owing to contraction of the longitudinal muscle, shrink to less than half its normal length. Dead or gangrenous gut, on the other hand, after losing its tonicity may measure much more than its normal. Another point of importance which should not be overlooked, is that successful resections of large portions of the intestine are much more likely to be reported than unsuccessful attempts, giving us, in all probability, much too low a mortality.

The history of my cases is as follows:

Case I.—W. J., male, aged twenty-nine, American, conductor. Admitted November 9, complaining of pain in the abdomen.

Present Illness.—Began one month ago with a generalized pain over the whole abdomen, paroxysmal in character, lasting from a few minutes to an hour. They occurred twice or three times a week and were associated with constipation. Bowels were moved with the aid of cathartics and enemas. Three days before admission, the patient was seized with an attack of pain similar in character, but much severer than his previous seizures. The pain eased somewhat the next morning, but there were frequent attacks during the day. These gradually increased in frequency until on the day of admission they occurred every few minutes. The pain is generalized, does not radiate to the back, shoulder, or any part of the abdomen or extremities. On the day of admission, patient vomited several times. Vomitus was greenish in color and of a sour odor. Bowels moved last before the beginning of the present attack, although on the night before admission, after taking an enema of warm water, the patient passed a few hard lumps of fæces. There has been no loss of weight. Appetite has remained good, and bowels have been regular until the onset of his present illness. At no time has he passed blood with his stools.

Past History.—In 1900, patient was thrown from his horse and apparently recovered. A few weeks later, while on a train en route to California, he was taken sick suddenly, became unconscious, and was carried to San Francisco, where he was operated upon. He was told that he had broken a blood vessel in his back, which was tied after a large clot was removed. He related, rather with pride, that he had torn open his wound on the day after the operation. He was very sick, and recovered only after a prolonged convalescence. His appendix was not removed at this operation. The wound was, from his description, drained for some time.

Family History.—Negative.

Physical Examination.—Negative, except for abdomen. Abdomen slightly distended. There is an irregular scar 6 cm. long, 3 cm. outside the linea semilunaris, midway between the anterior superior spine and the costal margin. The cicatrix has the

appearance of resulting from a suppurating wound. There is a slight fullness between the scar and umbilicus. Abdomen otherwise symmetrical. Respiratory movements present. No visible peristalsis or tumor masses. Panniculus poorly developed, so that abdominal musculature stands out clearly. Flanks symmetrical. Liver dullness extends from upper border of seventh rib to a point 3 cm. above costal margin. Edge of liver not felt. Stomach tympany not increased. During examination there are numerous attacks of pain, during which the knees are promptly flexed, but no peristalsis is visible. There is general abdominal rigidity, the right side being more tense than the left. Between the attacks the abdomen is softer, but no masses are palpable. No constant muscle spasm; deep palpation sometimes elicits spasm, and at other times not. No particular tenderness over appendix, gall bladder, or sigmoid. Pain seems generalized. Percussion much more painful than palpation. Abdomen everywhere tympanitic, except in the flanks, where the note is somewhat flat. No movable dullness.

Rectal Examination.—Prostate of normal size and consistency; not tender. Cul de sac filled with distended intestines. No inflammatory masses felt. Neither side tender to touch.

No hernia of linea alba. No inguinal, femoral, umbilical, perineal, or sacral hernia. No hernia in Petit's triangle.

Genitalia negative. No nodules on tibia. Reflexes normal.

Leucocytes 10,200. Temperature 99.4° F.; pulse 80, respiration 28.

Urine shows nothing abnormal.

From the history of the case, the possibility of neoplasm was thought of, although owing to his age it seemed more probable that he was suffering from a partial obstruction due to adhesions resulting from previous operations, although they had not given him the slightest trouble until the onset of the present illness.

A rectal tube was passed and a high enema of hot oil was given. Some gas and a little fæcal material was passed. An hour later a stomach tube was passed full length, and the enema repeated and a small movement obtained. There was no blood, and the fæces were well mixed with oil.

November 10. Patient has had two spontaneous movements, and is resting quite comfortably. An exploration was advised while the patient was in good condition, and accepted.

November 11. *Operation.*—Median incision at the level of the umbilicus. The ileum in the entire right upper quadrant was found matted together by firm, well-organized adhesions, which also bound it to the abdominal wall in the neighborhood of the old scar. The ascending and first part of transverse colon could not be reached owing to the adhesions. Cæcum was free and appendix normal. To facilitate the liberation of the adhesions, the old cicatrix was excised and the peritoneum opened midway between the hepatic flexure and cæcum. The ileum was carefully dissected free from the abdominal wall, and adjacent adherent loops liberated. In many places the union was so intimate that the muscle coat of one loop was injured, and once a small hole was torn in the bowel. This was immediately closed with a purse string suture, reinforced with several mattress sutures. Approximately seven feet of small intestine were involved in this mass of adhesions. Several stenoses and loops matted togethed in U shapes were found. As soon as the colon was uncovered, further palpation revealed a tumor mass in the transverse colon, just distal to the hepatic flexure. The tumor had a sharp constriction in the center, suggestive of an annular carcinoma. Adhesions made the palpation of the glands in the mesocolon uncertain. For fear of a recurrence of the adhesions in the small intestine, or necrosis of the intestinal wall where the muscular tunic had been injured, it was decided to resect the entire lower seven feet of ileum, together with the cæcum, ascending colon, and half of the transverse colon. A well-nourished point of healthy ileum was selected and the end invaginated, as in the treatment of the appendix stump. The mesenteric vessels were caught between clamps and divided, where possible, and ligated with fine silk by transfixion. The division and ligation of the branches of the superior mesenteric, ileocolic, colica dextra, and colica media to the middle of the transverse colon followed, although this stage of operation was rendered difficult by the presence of chronic enlarged glands, which were probably a residue of the old peritonitis. The cæcum and ascending colon were then freed by incision of the lateral reflexion of the mesocolon.

Finally, the gastrocolic omentum was incised, bleeding points ligated, and the transverse colon freed from the stomach up to the point selected for the anastomosis. Here the colon was divided, cauterized, and invaginated, as in the treatment of the appendix stump. The lower end of the ileum was then laid beside the transverse colon and a lateral ileocolostomy performed by means of the intestinal scissors, which I have described in another paper. The anastomosis was accomplished without a leak. The cut edge of the mesentery of the small intestine was held to the cut edge of the transverse mesocolon by the anastomosis. Sutures were unnecessary, owing to the overlapping. It was impossible to cover the peritoneal defect left by the ascending colon with the peritoneum and ascending mesocolon, owing to the inelasticity of the peritoneum, due to the old adhesions. The median wound was closed in layers, and the site of the original wound by through and through silkworm gut. A cigarette drain was passed from this wound down to the denuded area.

The resected portion of the small intestine measured 204 cm. collapsed, and 215 cm. distended. The firm adhesions prevented the usual great lengthening of the intestine when distended with fluid, as is usual in such cases. The resected portion of the colon measured 55 cm. On microscopic examination, the tumor proved to be a colloid carcinoma of the transverse colon, with metastases already present in the peripheral lymph spaces of the glands in the adjacent mesocolon.

The patient recovered from the ether rapidly, but was restless and complained of a great deal of pain. After morphine he seemed more comfortable. Maximum temperature 99.6° F., pulse 100, respiration 28.

November 12. Patient complains of severe pain, which morphine does not seem to control. There has been continuous proctoclysis since the operation. This fluid consisted of 15 per cent glucose in normal saline. The glucose was boiled and rendered alkaline. We felt it desirable to give the patient some nourishment, if possible, from the time of operation. Very restless, and tosses to and fro in bed a great deal. Temperature 98.4°-100.8°F., pulse 90-100, respiration 20.

November 13. Patient still complains of considerable pain in abdomen. Abdomen soft and not distended. Proctoclysis continued. Albumen water started and well borne, as the patient was suffering from thirst. During the evening the bowels moved spontaneously. Small dark fluid stool. No blood. Temperature 98.4°-99.2° F., pulse 80-95, respiration 20.

November 14. Patient feels well this morning, but is still somewhat restless. No change was observed until this afternoon, when, while the nurse's back was turned, patient jumped out of bed and rushed to the window. Broke a pane of glass trying to climb out. Afterwards seemed somewhat irrational. This evening asked for whiskey and cigarettes. There are no signs of an alcoholic psychosis, although patient gives a history of being a heavy periodic drinker. During the day patient had eight movements. Temperature 97°-99.8° F., pulse 76-90, respiration 20.

November 15. Patient passed a very restless night. Still very restless; complains of pain, but in no particular spot. Abdomen soft and not distended. Morphine and codein do not seem to control him. Diarrhœa continues. Movements becoming more frequent. Patient is given soft carbohydrate diet. At 1 o'clock he was given 8 ccm. of paraldehyde on the assumption that his postoperative psychosis might have some relation to his deprivation of alcohol. He immediately vomited violently and complained of

sharp pain in the epigastrium. His pulse rose rapidly from 80, at the time he vomited, to 120 at 8 P. M. At this time his temperature was 99.8° F., and respiration 25. Diarrhœa, twenty movements, some of which are voluntary.

November 16. Patient much worse this morning. Pulse remains high, temperature subnormal. Abdomen distended in both upper quadrants. Patient complains of great pain, chiefly in upper abdomen. Marked Hippocratic facies. Diarrhœa more marked, twenty-two movements, many involuntary; no blood. Dressing showed that the continual movements of the patient caused the sutures to cut partially through. Wound reddened, and some pus found around the drain. Median incision looks well. Temperature 96°-98.4° F., pulse 100-138, respiration 20-30.

November 17. Patient much worse. Temperature remains subnormal, pulse high. Toward noon he was almost moribund, and died at 7.30 P. M.

Permission could not be obtained for a complete autopsy, but consent was given to reopen the wound.

The median wound was healing superficially, but there was a small pocket of pus in the subcutaneous tissue about one of the catgut sutures. Omentum adherent to the line of incision. General peritoneal cavity free, peritoneum glistening and of good color. Anastomosis in good condition. No leak and very little reaction about it. A loop of ileum was found driven up between the left lobe of the liver and diaphragm. The loop is kinked, but there is not complete obstruction. It is covered with a fresh, heavy, fibrous exudate, which can be picked off, and shows two or three fairly large areas of beginning gangrene. On the right side of the peritoneal cavity, corresponding to the denuded area left by the ascending colon, is a walled-off area of local peritonitis into which the drain projects. There is some pus in this region. Probably the infection had travelled down the drain from the broken-down skin wound. There was no evidence of any compensatory process in the remaining portion of the intestine, for the removal of the segment of ileum and colon.

Remarks.—We could not account for the psychosis shown by the patient after the operation. It will be remembered that he behaved in a similar fashion after his operation in San Francisco. On the whole, he suffered remarkably little discomfort in the first three days after the operation, considering the nature and magnitude of the procedure. Save for his restlessness and continued motion, he was in excellent condition until the vomiting spell after the administration of the paraldehyde. It was undoubtedly at this time that the loop of the ileum was incarcerated between the upper surface of the left lobe of the liver and diaphragm. This was indicated by the prompt change in his vital signs, although there was no complete obstruction, as was shown by the continuation of the diarrhœa. The distension in both upper quadrants the next morning is evidence that there was partial obstruction above the incarcerated loop.

Of special moment, at this time, is the fulminating diarrhœa which was inaugurated about fifty-two hours after the operation, and continued with increasing severity until the patient died. The stools were fluid, small in quantity, foul-smelling, but contained no blood. While in no way immediately responsible for the patient's death, the debilitating effect of the diarrhœa undoubtedly had an influence on his resistance and vitality. From the resection of the ileum, or the colon alone, no such violent reaction could have been anticipated. Indeed, in view of Monprofit's case, even the reaction to the combined resection seems excessive, although it must be remembered of Mayndl's case, where a less extensive resection of the colon was done, the patient died of inanition.

It may not be out of place here to recall Cannon's interesting work on the movements of the colon, in course of which he found that the waves, up to a point about the beginning of the descending colon, were predominatingly antiperistaltic, while in the remainder of the large intestine the peristalsis was directed towards the rectum. These results are confirmed by the observations made on human beings by means of the X-rays after the ingestion of bismuth meals. Under ordinary circumstances, the contents of the stomach are found in the cæcum, about five or six hours after the meal is taken. Then they are found chiefly in the cæcum, ascending colon, and transverse colon, until about twenty-three hours after the meal, when they are deposited in the rectum. It will be seen, then, that we removed not only 204 cm. of the lower end of the ileum, but practically all of that portion of the colon where the intestinal contents remain longest.

In cases reported by the Mayos, where similar segments of the colon have been removed, no mention is made of a subsequent history of violent diarrhœa, and particularly Arbuthnot Lane's series of resection of the entire colon have shown, according to Lane, a violent post-operative vomiting as the single serious consequence of the operation. Harley's studies on the metabolism of dogs, from which the large intestine had been removed, reveal few disturbances of the equilibrium between intake and excretion, except in an increase in the elimination of water. Fat absorption is unaffected, while the observation on the nitrogen elimination varies; in one animal it is increased, and in another remains unaffected. Simple short-circuiting operations teach us nothing in respect to the conditions we are dealing with, as the intestinal contents in these operations tend to follow the usual course which the food takes. Even an anastomosis of the ileum with the sigmoid, where a complete stenosis exists, might still allow the food delivered into the colon to be carried back into the cæcum by antiperistalsis.

Fantino, after the death of his patient from inanition due to the resection of 300 cm. of ileum, drawing conclusions from another patient on whom, owing to error, he had created a sort of vicious circle while short-circuiting the entire colon and about 100 cm. of ileum, by reversing the anastomosis, suggests this as a regular procedure in cases of extensive resections of the intestine, because his patient stood the operation so well. He believes that, in this way, we might keep the intestinal contents long enough in the remaining segment of gut to allow the completion of the digestive processes.

Case II.—The second case is included in this series, notwithstanding the fact that only 100 cm. of the ileum was resected, but owing to the fact that the small intestine in infants of this age is only nine feet, the resection of 100 cm. is equivalent to the arbitrary limit of 200 cm. taken in adults.

A. K., aged 11 months, male. Admitted December 14, 1910; the mother states that the child is suffering from stomach and bowel trouble.

Present Illness.—For about 4 months the child has been suffering from a mucous entercolitis. The condition has apparently become progressively worse up to the present time. About one month ago the child was taken from the breast and given artificial feeding. Vomits occasionally. Has given evidence of frequent colicky pains. This afternoon, without any particular increase in the severity of the symptoms, the child had a stool mixed with blood and mucus. It was on this account the infant was brought to the hospital.

Past History.—No previous illness; normal delivery; weight at birth 10 pounds.

Physical Examination.—Patient is a fairly well developed baby, weighing 16 lbs., 14 ozs., somewhat anæmic in appearance; sits up well. Has a distinctly anxious expression, but gives no evidence of acute pain; climbs around on the bed during examination. No enlargement of cervical glands. Anterior fontanelle nearly closed. Heart and lungs negative. Abdomen slightly distended. No visible peristalsis or tumor masses. Abdomen perfectly soft. No general abdominal rigidity. Liver dullness not increased. Palpation of upper abdomen negative. No masses felt in the right iliac fossa. Extending up out of the pelvis toward the left iliac fossa, in the region of the sigmoid, is a small rounded tumor, not long enough to be definitely sausage-shaped. Tumor is apparently not tender, but palpation is followed by the appearance of an intestinal pattern with visible peristalsis. No moveable dullness. During the examination a muco-hemorrhagic stool of about 20 cc. was passed. Rectal examination revealed a tumor very much like an elongated cervix. The lumen at the apex of the intussusceptum felt exactly like the external os, and the finger could be freely passed between the intussusceptens and the intussusceptum. Straining followed the digital examination, resulting in the prolapse of about 8 cm. of the intussusceptum. Temperature 99.8° F., pulse 100, respiration 28. Urine showed trace of albumen and occasional hyaline casts. Immediate operation for the obvious condition of intussusception was advised and accepted.

Operation.—Median incision 15 cm. long, extending both above and below the umbilicus. The exploration showed the invagination of almost the entire lower half of the ileum, cæcum and colon into the sigmoid. The intussusception could be reduced to a point at about the middle of the transverse colon, when gangrenous intestine began to appear. In order to obtain a healthy intestine for anastomosis, it was necessary to resect 100 cc. of the ileum, cæcum, ascending colon, and one-half of the transverse colon. Owing to the collapse of the patient as soon as the abdomen was opened, anæsthesia was suspended, and the operation continued hurriedly without any further administration of ether until the incision was closed. The mesenteric vessels and mesocolon were ligated by transfixion, and the intestine freed to the point of anastomosis. Owing to the distension of the small intestine, an end-to-end anastomosis, by means of the Murphy button, was easily accomplished, and the defect in the mesentery and mesocolon was sutured together and the abdomen closed without drainage.

Examination of the specimen showed that the apex of the intussusceptum, projecting from the anus, was formed by the ileum at a point about 70 cm. above the ileo-cœcal valve, and the intussusception was one of the ileo-cœcal variety. Measurement of the specimen after the operation showed that 100 cm. of ileum and approximately 18 cm. of colon had been resected.

December 15. Temperature has risen to 101.6° F., pulse 160, and respiration 30, since the operation. Six muco-hemorrhagic stools were passed. Child appears to be in fairly good condition.

December 20. Condition of the patient has been serious since the operation. Pulse has averaged about 130. Axillary temperature between 98.4° and 100° F. There have been from eight to nine muco-hemorrhagic stools a day. Child took very little nourishment, other than a small amount of milk the first four days after the operation. Drank copiously of water. A rectal drip of 10 per cent dextrose in normal saline was maintained for four days after the operation. Abdomen has been soft. Blood ceased to appear in the stools on the fourth day, but they remain mucous in character. Murphy button was passed this morning.

December 26. Rectal temperature has ranged from 100°-98° F.; pulse has dropped to between 100-120; respirations from 20 to 24, there now being on the average of 10 stools a day, with occasional streaks of blood. For the last three days the urine and fæces were collected and metabolism studied by my colleague, Prof. Underhill, to whom I am indebted for the figures presented. During this period the balance of intake and output is shown in the table at the end of the history. The diet during this period has been peptonized milk, 4 ounces every two hours, some of which was refused.

December 29. Weight, 15 lbs. 8 ozs. Child appears to be improving. Now takes about 1 pint, 10 ozs. of milk per day.

January 1, 1911. Vital signs have been practically normal for the last five days; all stitches removed and wound healed per primam.

January 4. Weight, 16 lbs. Stools average 6 to 7 a day, occasionally mucous in character.

January 10. Weight, 16 lbs. 8 ozs. Six stools per day. No blood since last note.

January 23. Weight, 17 lbs. 10 ozs. Averge 3 to 4 stools per day. No mucus.

January 28. Weight, 17 lbs. 14 ozs. Three good stools a day; no mucus. Discharged from the hospital.

On the 25th and 26th, a second series of metabolic studies were undertaken. The results with the former test are shown in the following table:

Dates	Per cent of diet N. in fæces	Per cent of diet fat in fæces	Per cent of diet carbohydrates in fæces	Test for lactose	Positive balance grams N. retained per diem
December 24, 25, 26...	15	21	1%	Positive	+2.70
January 25.....	16	8	4% *	Negative	+0.49
January 26	22	9	5% *	Negative	+0.35

* The cereal was passed in the stool in undigested form.

The diet has been increasing to about a pint of full milk a day, with a small amount of Cream of Wheat (breakfast cereal) or toast. The study of this table shows that, while the nitrogen elimination has increased slightly, the fat elimination is markedly decreased. The percentage of carbohydrates in the fæces in the second series of experiments appears normally high, but this fact is due to the passage of the cereal in an undigested form. Of great importance is the fact that, while a test for lactose was obtained at the first examination, during which the child was suffering from diarrhœa, there was no trace of it either January 25 or January 26 after compensation was established. The course of the case is somewhat complicated by the existing enterocolitis, before the appearance of the intussusception. As the number of stools had been but three or four a day before the operation, the increase is undoubtedly due, as in the animals we operated upon, to the shortening of the small intestine. Notwithstanding the loss of one-third of the ileum, together with a large portion of the colon, the child was able to neutralize the loss,

and showed a consistent gain in body weight, and a constant improvement in the condition of the intestinal irritability. The weight increase is shown in the positive balance by the retention of 0.49 and 0.35 grams of nitrogen in the two days of the second period. The retention of 2.70 grams per day during the first period, ten days after the operation, apparently indicates the desperate effort the child was making to maintain its weight during the most active period of the diarrhœa. At this time, the general nitrogen elimination was somewhat lower than during the second period, but the fat excretion was much higher. Unfortunately, we have no data from normal cases to compare with the conditions shown by this child. The absorption of the lactose reaffirms the observations made on animals, and other human patients, and indicates the value of such readily absorbable carbohydrates, as the simple sugars, in the diet of these cases as well as the importance of employing them for nutritive enemata, as was done in both of our cases.

In this series of fifty-eight cases there were nine deaths, giving a mortality of a little over 16 per cent. While most deaths from the resection occurred where 274 cm. or more were removed, nevertheless 510, 520, and 540 cm. have been successfully taken out. In a variety of pathological conditions involving the small intestine, it would appear that the removal of portions of the ileum measuring 275 cm. is relatively safe. Schlatter's case, where only 192 cm. were resected, Dreesman's, where the amount removed was only 215 cm., and my own, gave much severer metabolic disturbances than the cases of Storp, Nigrisoli, and Brenner, the maximum successful resections in the literature. It is, then, natural to seek the explanation of these differences, partially in errors in measuring the length of the resected portion of the gut, but more probably in such accessory and important factors as the age, the condition of the patient, the total length of the intestine, and the effect of the pathological condition upon the patient's strength and resistance. Obviously, the result of the operation depends upon these features of the case as well as the length of the resected segment.

The clinical manifestation of the metabolic disturbances caused by an abbreviation of the intestine consist largely in a diarrhœa which, in the majority of instances reported, was only slight in degree, the patient ordinarily having two or three soft or fluid movements a day. These stools were often fatty in character, indicating the inability of the patient to absorb the fatty content of the food. In other cases, the disturbances were moderate in degree and, in still others, like the cases of Pauchet and myself, the diarrhœa was of a fulminating character. Another type of reaction to the removal of the gut was shown where the patients recovered from the operation, but suffered from such profound limitation of the power of absorption that they died later of inanition. The cases of Mayndl, von Eiselsberg, and Fantino were examples of this type, all of which lived about a month after the resection of the intestine. Brenner's case, first reported as successful, finally died of inanition 2½ years after the operation.

Morphological Changes Following the Operation.

In several cases, experimental investigations upon resection of the small intestine have been carried out during the past fifteen years. The first of these were the researches of Senn, whose paper, unfortunately, was not available to me. He gives the limit of resection as 33 per cent of the small intestine. To remove more than this amount is a dangerous operation that will result in marasmus, and terminate sooner or later in death. Senn, according to the authors who have quoted him, also described a compensatory hypertrophy following the removal of the gut. Later, Trzebicky undertook to establish, by means of experiment on animals, the limit of resection of the small intestine. He removed, in a series of dogs, 25, 50, 75, 100, 150 and 200 cm. of the combined jejunum and ileum. In one series, he removed the upper, in another, the middle and in a third, the lower portion of the gut. Trzebicky judged the metabolic disturbances from the post-operative loss of weight in his animals. His results led him to conclude that only 50 per cent of the combined ileum and jejunum could be removed without serious metabolic disturbances, and that the excision of 75 per cent led to such profound changes in the digestive apparatus that life was impossible. At the autopsies on his animals, he found, when large percentages had been removed, a dilatation of the intestines and a disappearance of fat. A compensatory hypertrophy could not be found by this author. In applying his results to the human intestine, Trzebicky stated that not more than 280 cm. should be excised, as the total length of the combined ileum and jejunum in man was, according to his measurements, from 561 to 870 cm. He found, furthermore, that the removal of the jejunal end of the intestine led to more profound losses in weight than when the lower end of the gut was resected.

Monari, in 1896, by a series of operations on dogs, endeavored to establish the limits of resection in the gastro-intestinal tract. He removed the entire stomach of a dog and found no interference with the metabolism. Then he took a series of five dogs from which he removed 186, 170, 249, 215 and 200 cm. of the small intestine respectively. The operation, in spite of a rich diet, was followed by a period of denutrition, which was characterized by profuse diarrhœa, followed by improvement with frequent relapses. The dogs from which 186 and 200 cm. had been removed died within three months. The autopsy showed great loss of weight, atrophy of the muscles, absence of fat and anæmia. In the first dog there was 15 cm., and in the second there were 12 cm. of intestine, exclusive of the duodenum, remaining. The other three dogs lived eighteen months, but never regained the weight they lost after the operation. They had respectively 19, 16 and 20 cm. of small intestine remaining.

From the microscopical examination of the specimens obtained from these dogs, Monari states that the mucous membrane was twice the thickness of the control animal. The villi were more numerous and larger, and the cylindrical epithelium, with which they are clothed, showed an increase in the number of goblet cells, which at the base of the villus

are larger and more numerous than in the norm. The lymph follicles are enlarged, and likewise the circular layer of muscle, while the longitudinal coat showed no change. De Filippi, whose results were published separately, studied the changed metabolism in the dog from which 190 cm. of intestine had been removed, and found no changes, except in a diminished fat absorption. From his work Monari believes that 50 per cent of the human intestine can be removed without the danger of metabolic disturbances.

A most interesting recent contribution to the study of extensive intestinal resection is afforded by the experiments of Evans and Brenizer, who resected 33, 37, 41 and 50 per cent of the combined jejunum and ileum with recovery, and the discovery of a more localized hypertrophy, particularly marked in the neighborhood of the anastomosis. The resections were followed by another series in which 76.1, 84.6, 86.5, 87.3 and 92.0 per cent of the total mesenterial intestine was removed. The first two animals of the series recovered, while the last three died of inanition, after living thirty, fifty-one and ninety-seven days respectively. The last animal of the series was very fat, which probably enabled him to live off his own tissues for the greater length of time. In the last animals, no hypertrophy was noted, these being cases where the resection had exceeded the limit where a compensation could be established. Certain of our own animals showed a similar behavior, which is not unlike the human cases that made an operative recovery, and died later of inanition. These authors conclude that an animal can practically always survive the removal of from one-third to one-half of the combined jejunum and ileum, but that resections greater than this may exceed the limit for which a compensation can be made.

In the autopsies upon our own animals, nothing was found of an abnormal nature outside of the intestine itself. Dogs Nos. 1, 2 and 10 were fairly well nourished, while No. 9 was thin. The macroscopic changes in the intestines in Nos. 1, 2 and 10 were all practically alike. Careful measurements from the landmarks left at the time of operation showed that there had been no increase in the length of the intestine. Within the small limits of error that one might reasonably allow, the dimensions were the same. If any real lengthening had occurred, it was so slight that it could not be distinguished from a possible error in measurement. The intestines showed a marked increase in the transverse dimensions, which to the naked eye appeared to be about twice the size of the gut at the time of operation. This increase was confirmed as the intestine was taken from the body and compared with the piece that was removed at the operation. In all cases except No. 9, in which the writer did not see the autopsy or control the preservation of the specimens, the hypertrophy varied between 30 and 100 per cent. It involved both the stomach and the cæcal end, although the relative difference in the size between these two portions of the intestine was preserved.

There is, however, apparently a limit beyond which a hypertrophic response can be obtained, where simply an intestinal incompetency is established and the dogs die of slow starvation, prolonged and modified by the amount of food they can assimilate through the abbreviated gut. In such cases, the compensatory hypertrophy is absent. In other cases, the response may be partial, but the dog may never gain its full weight, and hence be only a partial recovery. Dog No. 12 is an example of this type. The hypertrophy was not nearly so marked as in the Dog No. 2, and the partial compensation is indicated in the functional inefficiency of the intestine as shown by Professor Underhill's metabolic determination in contradistinction to those obtained by Erlanger and Hewlett on Dog No. 2, under conditions of an average diet.

It was difficult to ascribe a cause to the transverse hypertrophy, and the failure of the intestine to enlarge markedly in its longitudinal dimension. The only plausible interpretation appeared to lie in the mesentery. The mesentery, while providing for the normal elasticity of the gut, naturally holds the intestine somewhat fixed in its longitudinal dimension. This might be looked upon as the factor involved, although in such an elastic organ a slight lengthening of the gut may have been present and escaped observation, owing to the contraction of the longitudinal layer of the tunica muscularis. If this were the case, however, the increase could not have been in excess of 15-30 cm., the usual probable error in careful measurement.

In Dog No. 12, where the small intestine was short-circuited, the differences between the two segments are beautifully shown (Fig. 1). The functional segment is seen markedly hypertrophied while the short-circuited portion appears about one-half its size. The transverse folds, due to the contraction of the longitudinal muscle, are seen in both sections of the gut. In all other animals, no evidences of compensation or change were observed in the stomach or large intestine; both remained macroscopically normal. In this case, however, there is a marked dilatation of the stomach, with an almost complete atrophy of the omentum, but the large intestine appears normal. Sections of the stomach in these animals show that the parietal cells are considerably more prominent than the chief cells, the histological picture resembling not a little that given by Heidenhain for starving animals. No other changes were observed in the stomach. Microscopic study of the colon in Dog No. 12 showed it to be of normal structure and thickness, making it evident that the colon had undergone no morphological changes to compensate for the functional removal of the small intestine.

It might be suggested that the difference in size between the two segments of ileum in Dog No. 12 was partially due to an atrophy of the functionless portion of the gut, especially as Cunningham has described such changes after short-circuiting for physiological experiments. Plant, who kept a dog alive two and a quarter years with a short-circuited loop which he had used for the study of fat absorption, found absolutely no evidences of atrophy. The sections of the short-circuited ileum of Dog No. 12 were the most perfect I have seen, and showed absolutely no evidences of degeneration of any sort. Furthermore, the comparison of the size of the gut with that of normal dogs revealed no changes other than in the

remarkable clearness of the histological picture. This, I believe, to be due to the absence of fats undergoing absorption which tend, when the intestine is thrown into the fixing fluids, to cause a separation of the epithelium from the stroma of the villus.

Monari states that there is a regeneration of the villi, that is to say, that they are more numerous after the operation than before. This appears to be a random statement, for only by the most accurate methods of observation could one say definitely that there was an increase in the number of villi. At the outset, I may say that I expected to find a regeneration of the villi, for, according to the manner of their development, it seemed like a simple method of providing for an increase in the epithelial surface of the intestine. In order to prove or disprove a regenerative process, I counted the villi and estimated the area of the intestine removed at operation and autopsy. The number of villi in a square millimeter were counted a great many times in each 10 cm. of intestine and the average taken. From this, the number in each 10 cm. of intestine were computed. Like the length of the intestine, the total number of villi varied in different animals. In the series of animals from which I computed the number of the villi, including not only our operated dogs, but several normal ones as well, the total varied between 800,000 and 1,200,000. The number does not vary to any great extent between the upper and lower portions of the intestine, although the cæcal is much smaller than the stomach end of the gut. This indicates that the villi are smaller in this region, a fact which can be proved by a comparison of villi from the two sources in the same animal, or demonstrated by sections of the healed suture in these extreme resections, where the upper end of the intestine is anastomosed to the lower. Here, where the two types are found on either side of the scar, on the duodenal side of the cicatrix they are about 50 per cent larger than on the cæcal side, if there has been an extensive resection of the gut.

In comparing the portions of intestine removed at operation with those obtained at autopsy, approximately the same number of villi were found in each 10 cm. of intestine. In the same unit of area, however, only half as many were counted in the hypertrophied intestine as in the piece removed at operation. Inasmuch as there had been an increase in the total area of each 10 cm. of nearly 100 per cent, the villi had naturally not increased in number, but had simply increased in size. In this way, it was possible to exclude positively at least any extensive regeneration of these structures which Monari believed took place. Although, as was shown later, the hypertrophic process involved the submucosa and muscularis as well as the mucosa, this was not apparent from a macroscopic inspection of the intestine. It gave the appearance, however, that the operation had yielded an intestine that was magnified about one diameter. This hypertrophy was more apparent in the upper than in the lower end of the gut.

To determine the exact effect of the resections upon the intestine itself some accurate method must be employed. The comparison of sections by the eye must be supplemented by a mathematical registration of the differences in the intestine before and after the operation in three dimensions. Monari simply used a control dog and, in this way, could not exclude the possibility of individual variation between his control and his operated animals. Accordingly, to obtain the desired comparison, and still to avoid all possible errors by the use of control animals, I reconstructed a portion of the intestine removed at the operation from the region of the upper suture in Dog No. 10. After the animal had lived a year and a half, another piece was reconstructed from the region just above the line of anastomosis, where the upper and lower ends of severed intestine had been united. In this way pieces were obtained that were not separated from each other during life by more than 5 cm. Observation shows that there are no differences in the structure of the intestine under these circumstances, although the intestine is smaller at the cæcal than at the stomach end, and that the several coats are not so large or well developed in the distal portion of the gut. Any differences, therefore, between these two reconstructions must have been caused by the operation, and the model made from the resected pieces would represent the normal conditions for that region of the intestine. Such a model shows a number of facts interesting in themselves as well as being of importance for comparison, for it represents the normal anatomy of this portion of the intestine; but it should be remembered that the description applies only to the dog's intestine. A glance at Fig. 2 reveals the following interesting facts. The normal villus can scarcely be looked upon as having a definite shape, as it is a more or less plastic element, influenced in its form by factors in its environment and in its architecture. The profile picture of a villus seen in sections, for example, gives no real conception of its form, as one must reconstruct many of them in three dimensions to appreciate the extreme variability of their contours in a fixed condition, and to discover the factors that determine its shape under these conditions. Under perfectly relaxed conditions of the tunica muscularis, as well as the muscle bundles within the intestine itself, the form of the villus would probably be columnar with rounded ends. As soon as the musculature of the intestine contracts, or when the intestine is thrown into the fixing fluid, the villus alters this form. This alteration, due to the contraction of the muscular wall of the intestine and the intrinsic musculature of the villus, does not represent an abnormal condition, but records permanently conditions that occur regularly in the intestine. The form of the villi has been variously described as cylindrical, fusiform, club-shaped, etc., but a glance at Fig. 3 shows that there are no constant shapes, as the form is largely an adaptation to external pressure and all of these types may be found in the same region. This pressure is exercised under normal conditions by a contraction of the muscular coats, which may, naturally, act in one direction or the other by the single action of either the outer or inner layer of the tunic separately, or in both directions at once by the simultaneous contraction of both sheets of muscle together. In such a specimen, the villi always fit into each other, leaving only a small space between their epithelial surfaces. Club-

shaped, cylindrical, fusiform villi, and those with pointed ends occur side by side, closely packed together, taking on a form to fit the space they have to occupy. At times they are triangular in cross sections and may be folded or grooved to fit adjacent villi that impinge upon them. When one finds a villus with pointed ends, ordinarily there are club-shaped elements next to it. In general, the end toward the submucosa is smaller than the end toward the lumen of the intestine, a relationship, however, due to the contraction of the combined muscular coats. When the longitudinal muscle bundles within the villus contract, the epithelium on the surface of the villus is thrown into a series of transverse folds (Fig. 3). This illustrates excellently the pump action of the villus, which is a notable factor in aiding the movement of the intestinal lymph. By the contraction of the musculature in its stroma, the central lymph space of the villus is emptied into the submucosal plexus, where its return is prevented by the valves situated at that point. Villi in a state of contraction are shown by the folding of the surface epithelium.

In many cases, the ends of the villi are rounded, while in others they are pointed and irregular. Likewise the sharp contraction of the intrinsic musculature of the villus as it is thrown into fixing fluids, often draws the stroma away from the epithelium and allows the latter to hang loose, like the finger of a partially withdrawn glove. By some investigators this has been considered a normal relationship, but it is obviously an artifact, as the stroma draws the membrana propria away with it and allows the epithelium to hang free and loose. Such free tips of epithelium are nicely shown in the model represented in Fig. 2. It may be well to observe, however, that such pictures are much more readily obtained during digestion, for the accumulation of the fat globules beneath the epithelium during absorption seems to facilitate the ease with which the stroma may be retracted from the epithelium. Instances where the stroma projects into the epithelial tips, however, are not abnormal. The average size of the villi in the same region of the intestine is constant, although their power of contractility gives them, under fixed conditions, a slightly different caliber. Unfortunately, owing to the scale selected for the model, it was hardly possible to show the relationship of the crypts to the villi. They are represented by the solid portion of the model under the villi.

After the resection of large portions of the intestine, say from 50 per cent to 70 per cent of the entire small intestine, or from 60 per cent to 83 per cent of the combined ileum and jejunum, very marked changes take place in the structure of the remaining portion of the intestine. These modifications are shown in the model represented in Fig. 3, which was made from a portion of the intestine of the same dog as Fig. 2, and was not situated more than three or four centimeters from it before the resection of the intestine took place. Thus all of the differences shown by this preparation are the direct results of the operation. At the first glance, the enormous hypertrophy, which reaches about 100 per cent, is seen. Not only the villi are enlarged, but also the portion of the mucosa forming the crypts shows an increase in size approximately equal to that of the villi. So far as the form of the villi are concerned, the relationships are practically the same. In the increase of the epithelial surface by the hypertrophic process, there seem to be a few more club-shaped villi, which may indicate a slightly greater increase in the mucosal as against the muscular coats of the gut, or may be due to a greater degree of contraction of the latter. In the hypertrophied specimen, great irregularity is observed in the form of the villi, but, as in the normal intestine, this represents an adaptation on the part of the villus to the space which its neighbors allow it to occupy. There is, naturally, the same interaction of the individual villi upon each other's form. Numerous longitudinal folds occur in the villi near the base to allow them to fit in with the adjacent elements, and, where the longitudinal bundles of muscle in the villus are contracted, the epithelial surface is thrown into a series of transverse folds, giving it a corrugated appearance. In the hypertrophied specimen, this condition illustrates the pump-like action of the villi even better than the contracted elements in the normal intestine.

The microscopical changes that take place in the intestine after the resections, may be seen in the two figures drawn from sections of the gut before and after the operation. Fig. 4 is taken from the upper end of the resected portion of the intestine removed at the first operation, while Fig. 5 is from the portion of the ileum just above the first suture; that is to say, the tissue from which the sections were cut, like that from which the reconstructions were made, was situated in the same segment of the gut before the operation was undertaken.

The hypertrophic process induced by the resections involves all the layers of the intestine, but it is more patent in the tunica mucosa than in either the submucosa or muscularis. In the mucosa, the hypertrophy occurs in the region of the crypts as well as in the villi. The latter show an increase in the amount of their stroma, although it maintains the same characteristics as the stroma of the normal villus. The reticulum framework is a little denser and its nuclei are more numerous, otherwise the connective tissue is unchanged. The longitudinal bundles of smooth muscle are proportionately enlarged, and the vessels appear more tortuous. On comparing the epithelium of the hypertrophied villus with the control specimen, it is observed to be distinctly higher than normal, the hypertrophy reaching, perhaps, 30 to 50 per cent in excess of the cell's original size. The nucleus also takes part in this process with a slight increase in size, but otherwise, the cell retains all of its usual characters, such as the granular protoplasm and the cuticulated border toward the lumen of the intestine. Goblet cells are numerous about the base and sides of the villus as in the control specimen, but there is no increase relatively in the number of these cells, such as Monari described, although with enlarged epithelial surface there is a numerical excess over the control specimen. No mitotic figures are seen in the epithelium covering the villus.

It is not possible to make out great changes in the stroma of the region of the crypts, but like the epithelium of the villus, these elements themselves are both hypertrophic and hyperplastic. The chief increase is in the length of the crypts,

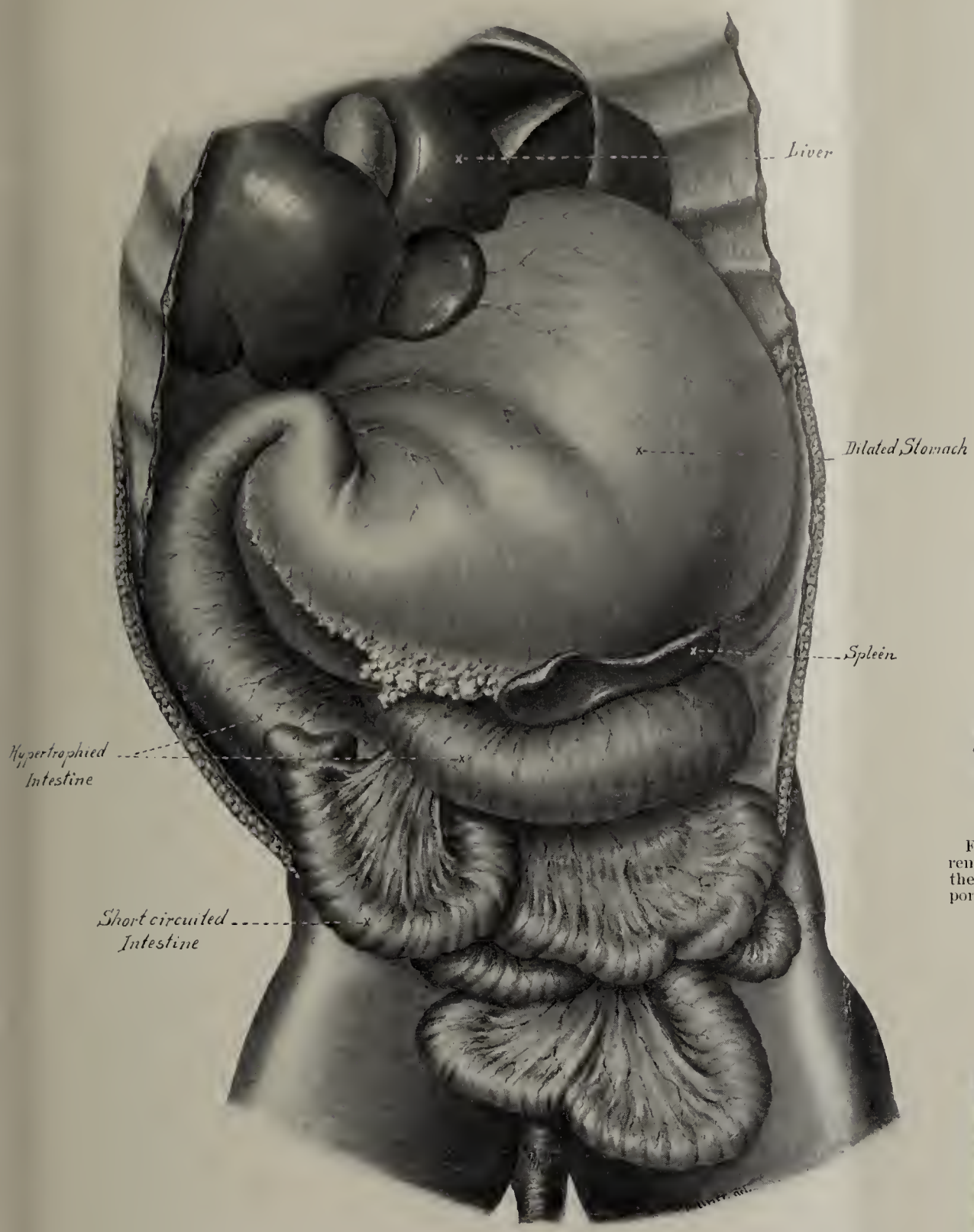

FIG. 1.

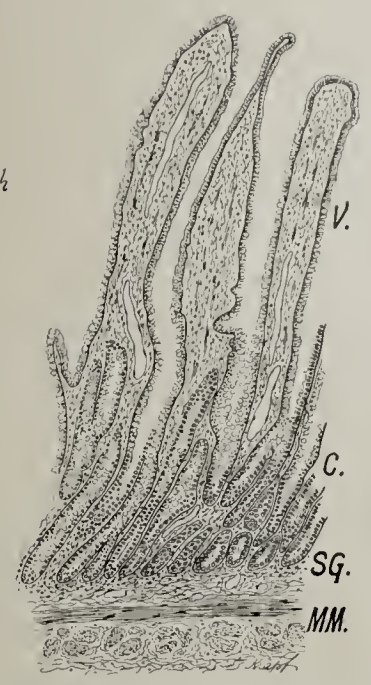

FIG. 4.—Section of the intestine removed from Dog No. 2, taken from the stomach end of the resected portion in the first operation.

FIG. 5.—Section of the mucosa taken from the duodenal side of the upper suture in Dog No. 2; that is to say, from the same region of the intact intestine as the section shown in Fig. 4.

FIG. 2.—Reconstruction of a portion of the duodenal end of the intestine removed at operation from Dog No. 10.

FIG. 3.—Reconstruction of a portion of the intestine from the same animal as Fig. 2. Taken from a region just above the healed intestinal suture. Before the operation, the pieces of tissue from which Figures 2 and 3 were taken were separated from each other by not more than a few centimeters. Reconstruction on the same scale as Fig. 2.

and in the presence of occasional cystic dilatations at their extremities. These ampullæ-like widenings rarely exceed four or five times the diameter of the crypts, and ordinarily show little evidence of pressure or pressure atrophy, although in one or two instances I have observed points where epithelium was flattened to a third of its normal height. These cysts are filled with a coagulated granular mass and desquamated degenerating cells. The proportion of goblet cells has not increased. In the lower half of the crypts there are numerous karyokinetic figures, probably representing the regular regeneration of the epithelium of the villi and the crypts, according to the observations of Bizzozero and Heidenhain.

In Dog No. 1, however, the karyokinetic figures are much more numerous than in the other three cases. This may, of course, represent only a very active regeneration, but it seems quite possible that it is associated partly with the hypertrophic process, for, in this case, I have also found occasional mitotic figures in the stroma of the villus. This dog was killed before the total compensatory increase in the epithelial surface was established, and thus the excess of karyokinetic figures over those that are present in Dogs Nos. 2 and 10, can be explained. It is extremely difficult to form an opinion concerning the changes in the stratum fibrosum and the stratum granulosum, for they vary to a marked extent with the degree of distension of the gut, but it is probable that, in common with the submucosa, these layers are somewhat enlarged.

The muscle tunics have distinctly hypertrophied, but of the two, the inner circular layer is larger when compared with the control specimen. This is in accord with Monari's observations. The Peyer's patches have also taken part in the general enlargement, and in Dog No. 1 evidences of cell division are occasionally found. The enlargement of these structures are by no means proportional to the hypertrophy of the mucosa, however, in my specimens, but owing to the impossibility of distending both portions under exactly the same pressure, this point is of no moment, as the comparison cannot be made absolute.

After the consideration of the morphological and metabolic changes resulting from a shortening of the small intestine, it is now possible to consider these modifications of structure and function in their relations to each other.

In trying to determine the cause of the hypertrophic process that occurs after the extirpation of a large portion of the gut, there are a number of factors to be taken into consideration. In the first place, there is no question that more mechanical work is done by the portion that is left. The simple mechanical effect, however, of the increased amount of food and water taken, as evidenced by the ravenous appetite and great thirst displayed by the animals after the operation, seems inadequate to explain the change, for these, like the normal appetites, are more probably simply symptoms of a tissue thirst and a tissue hunger induced by the reduction of the normal absorption of food stuffs. If the term "work" is used in the sense of an increased functional activity, then, to be really explanatory of the hypertrophic process, it must be analyzed into its several factors.

As was shown by the investigations of Diliberti-Herbin, the immediate metabolic effect of the operation is to diminish, to a marked degree, the absorption of fats and nitrogenous substances. According to Vitali's observations there is, in all probability, also an initial decrease in the absorption of carbohydrates, whereas after the compensation is fully established by the hypertrophic process, these food stuffs are completely utilized. This diminished absorption or increased excretion with its consequent destruction of the normal balance between ingestion and elimination, makes it essential, if the nutrition of the animal is to be maintained, either for the remaining portion of the intestinal mucosa to improve in the efficiency of its power of absorption, or else to proliferate and increase its area as a compensation for the lost portion of the gut.

As we have seen, the second process takes place and we may say then, that the diminished absorption of fats, nitrogenous substances, and carbohydrates causes a proliferation of the intestinal mucosa, and at the same time of the other coats of the intestine. As time passes, there is a gradual decrease in the excretion of these substances (Diliberti-Herbin) and with it goes hand in hand an increase in the absorbing surface of the intestine, as is shown by the findings in Dogs Nos. 1, 2 and 10. The metabolic disturbances may, under favorable conditions of diet and life, finally disappear, and the nutrition become practically normal (Erlanger and Hewlett, Dogs Nos. 2 and 10). When this condition is attained, we find that the mucosa in a dog with 70 per cent of the small intestine removed (Dog No. 10) has hypertrophied to the degree shown in Fig. 3.

This ratio between area of absorption and the degree of elimination proves positively that there is a relation between the area of the intestine and the nutrition of the animal. We may even go as far as to say that, under normal circumstances and average conditions of diet, there must be a minimal relation between the area of the intestine and the size of the organism.

The intestine, like other organs, probably rarely functions up to the limit of its capacity. Like the heart and other organs, there is a reserve power rarely called into use. This excess in the intestine may, perhaps, be measured by the resection of small portions, where the metabolic reaction is nil, or is buried in the normal variations. But when the limit of this reserve is reached, the diminished absorption involves the adaptative powers of the remainder of the intestine and a compensation for the loss is established in a hypertrophy of the remainder. In this case, the parallel between the hypertrophy of the heart and the hypertrophy of the intestine is perfect, although the functions and factors involved may be entirely different. Moreover, the comparison may be carried still further, for the adaptation, as in the heart, although admirably calculated to compensate for the loss, lacks the efficiency of the normal organ. Like a machine run to its full capacity, it is liable to break down. This was admirably shown in the case of Dogs Nos. 2, 9 and 10, where under favorable condition of diet and life, the hypertrophy secured

a functional adjustment like that of a normal dog. As soon as these favorable conditions ceased to obtain, the insufficiency of the adaptation became evident, and nitrogen and fat were eliminated in a much higher percentage than in a normal animal. If adjustment is too fine, as in Dog No. 9, the break leads to death, like a broken compensation of the heart, or to some such condition as the prolapsus recti, induced in Dog No. 10 by the profuse diarrhœa.

The history of the operations on the human intestine parallels in all respects the experiments upon our animals. Schlatter's case particularly, with the diminished absorption which persisted for almost two years, reached finally such a stage of compensation that his patient, an Italian, could eat the frugal diet of his people. In this case there is little question that the hypertrophic process was slowly taking place.

A last and most interesting point in connection with the functional adjustment produced by this hypertrophy lies in the relationship of the epithelial or absorbing surface of the intestine before and after adaptation has taken place. In Dog No. 10, from which the reconstructions were made, the hypertropy of both villi and crypts led to an increase of almost twice their original size. In this case 238 cm. of the intestine was resected, and the portion remaining, as shown at autopsy, was 96 cm., making a total length of 334 cm. In such more or less cylindrical structures, as the villi and crypts, an increase of 100 per cent in their size would lead to an increase of 400 per cent in surface. That is to say, the surface of the enlarged villus or crypt would be four times that of the original element.

Bearing this fact in mind, I have endeavored to compute the degree to which the compensatory hypertrophy restores the original epithelial surface of the intestine. A computation of this character, naturally, cannot be made more than generally accurate, but the figures indicate that the compensatory enlargement of the crypts and villi, when the process is complete, approximately restores the original surface of the intestine. That a hypertrophic mucosa, even should it have the area of a normal intestine, is not as efficient an agent for the absorption of the essential part of the digestive processes which are carried on in the intestine, is shown by the ease with which it becomes incompetent to do its work—a fact to which attention has been called above, in Dogs Nos. 2, 9 and 12.

It was noted in discussing the autopsy findings that the stomach and colon play no demonstrable part in the compensatory process. Barring conditions in Dog No. 12, where the stomach was markedly dilated, no changes of note occurred in these organs. Thus, there is a pretty definite basis for the view that the different portions of the alimentary tract exercise a fairly specific function, and while, as has been shown, an animal or a man may live without either stomach or colon, a certain amount of small intestine is necessary for the maintenance of life. Indeed, after the efforts at regeneration which the organism makes to restore lost parts of the intestine, it is probable that there is a definite ratio between the size of the organism and the epithelial surface of the intestine under ordinary conditions of diet and life.

This is made even more probable by the interesting experiments of Babák, who tested the question on frogs. Frog larvæ may be brought up either as herbivora or carnivora. Babák divided a large series of larvæ, feeding one group with a vegetable and another with a meat diet. The groups raised as herbivora invariably had larger intestines than those fed on meat. This indicates the influence of the diet on the size of the intestine, but might equally well be used to express the demands which the organism makes for a certain absorption surface, which may be demonstrated either by reducing that which it possesses or changing the nature of its diet to one less easily assimilated. Pauchet states in his paper that he intended to bring about a lengthening of the intestine of his patient by feeding a vegetarian diet. If, however, this idea were carried out without judgment, it might be made equivalent to a more complete resection of the intestine.

So far as the practical bearing of the researches upon animals with shortened intestines are concerned, the results do not justify us in establishing a limit of resection which may be definitely applied to the human intestine. Even the series of cases of extensive resection of the human ileum set no definite boundary which it is fatal to exceed, as the maximum measured instance in the literature, a case of 540 cm., was not only immediately successful, but caused astonishingly little metabolic disturbance, although the ultimate outcome was death from inanition two and one-half years later. From the experimental standpoint, this limit will not be established until the method of fractional resection is thoroughly applied, as the interesting work of von Haberer on the kidney shows. At present, even the results of primary resection are colored too much by such factors as the age and condition of the animal or patient, the length of the intestine and the functional efficiency of the mucosa. As a matter of fact, notwithstanding the effort of numerous investigators to establish this limit, its interest is only academic, and its application will only be of use in affording us, perhaps, indications as to diet and a probable prognosis of the case. These facts are shown by an inspection of the table of cases given above, when more than 200 cm. of the intestine was resected. In these instances, the procedure was never an operation of choice, as the extent of the resection was established by the pathological process and not by the surgeon. The surgical rule has been and will continue to be, the removal of the minimum amount of the gut permitted by the morbid condition, and the prognosis will depend chiefly upon the factors given above; namely, age, condition, resistance, nutritive efficiency, and the length of the unresected segment of the gut. To these factors might be added, as Fantino has pointed out, the ability of the remaining part of the intestine to inaugurate compensatory processes. There are, apparently, instances when portions of the intestines are functionally incapacitated some time before the necessity of an operation, a condition which would bring the case to the operating table with a partially compensated or hypertrophied intestine, and thus facilitate the subsequent compensation for the resected segment of the gut. Such a state of affairs would almost be equivalent to a fractional re-

section, where the hypertrophic process would be partially established before the limit of resection is reached.

Generalizations from our animal experiments might lead us to assume that 50 per cent of the human intestine might be removed, perhaps with severe nutritive disturbances, but with no probability of death. A study of the cases, however, shows the possibility of death from inanition where only 300 cm. have been resected. Mayndl's case, which died of marasmus after the removal of 284 cm., was possibly complicated by the cachexia caused by the carcinoma cæci which necessitated the resection. If we are justified in generalizing from these cases, we may say that there is not great danger in removing as much as 275 cm. of the small intestine, but that beyond that limit death from marasmus may occur. As a result of the operation, there is the possibility of severe nutritive disturbances after the resection of so small an amount as 198 cm., as is evidenced by the case of Schlatter. On the other hand, the resection of much larger amounts may yield relatively little post-operative interference with the metabolism, as is shown by Brenner's patient, from whom he removed 540 cm., but in the end, lead to inanition and death.

The metabolic experiments indicate that the diet in these cases should be rich and easily assimilated, but it should not contain too great a percentage of fats. The complete utilization of the carbohydrates of the diet suggests the advisability of increasing these elements of the food, especially in some easily assimilated and usable form, like the simple sugars.

Conclusion.

1. As much as 50 per cent of the total small intestine in dogs may be removed without fatal results. The animals may gradually return to a condition of practically normal weight and metabolism when maintained on the favorable diet under good conditions. Resections of 75 per cent and even more of the total small intestine may be survived, but such animals are not liable to show a true recovery, *i. e.,* a return to normal weight with the establishment of a good compensatory process.

2. At first, the animals suffer from a severe diarrhœa, ravenous thirst and appetite, and loss of weight, from which they gradually recover until conditions may return to those of a normal animal. They remain, however, extremely sensitive to unfavorable conditions of diet and living.

3. Metabolic studies on such animals show that there is a marked increase in the excretion of the nitrogenous, fatty, and carbohydrate elements of the food. The elimination may reach 66 per cent of the diet content. After compensation is established, on a rich, easily assimilated diet, digestion goes on as in a normal dog, except for an increase in the amount of intestinal putrefaction, as indicated by the amount of indican in the urine. An increase in the amount of fats in the food may lead to an increased elimination of nitrogen and fats to a point about 25 per cent above normal. The carbohydrates, on the contrary, are absorbed to a degree considerably above normal after the compensation is established.

4. The compensatory process consists in a hypertrophy as well as hyperplasia of the remaining portion of the small intestine. There is no regeneration of either the villi or crypts. Computation makes it probable that in favorable cases approximately the original epithelial area of the intestine is restored by the hypertrophic process.

5. As in animals, about 50 per cent of the small intestine may be resected without much danger of serious consequences in the majority of cases. The resection of smaller amounts may, however, be followed by severe metabolic disturbances, and even inanition and death. Human cases behave in general like the animals. They show similar metabolic disturbances. In one case there was distinct evidence of a compensatory process. No regeneration or hypertrophy has ever been reported in a human case. There are over fifty-eight cases reported in the literature where over 200 cm. of the small intestine have been resected. The mortality is 16 per cent, which is probably much lower than it should be, owing to the greater probability of successful cases finding their way into the literature.

6. The metabolic disturbances in human cases bear no definite relationship to the amount of small intestine resected. Five resections of over 400 cm. have recovered, while death from inanition has resulted from the resection of 284,289,300 and 350 cm., respectively. Profound digestive disturbances have resulted from the removal of 192 and 204 cm. of ileum. In human cases, factors like difficulties in measurement, the pathological condition, the total length of the intestine, and the resistance of the patient undoubtedly modify the result, and explain the apparent discrepancies between the amount of intestine resected and the subsequent metabolic disturbances.

7. The prognosis in human cases should be guarded. Apparently successful resections may, for lack of suitable compensation, succumb ultimately to a slow process of inanition.

8. The experiments and the series of human cases emphasize the specific function of the three segments of the gastro-intestinal tract. Neither the stomach nor colon is able to compensate for the loss of large portions of the small intestine.

9. Resection of the human intestine is almost never an operation of choice. The surgical rule has been, and will continue to be, a resection of the minimum amount allowed by the pathological conditions. From the metabolic studies, it would seem wise to give these patients a rich and easily assimilated diet, poor in fats and relatively rich in carbohydrates.

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THE BEHAVIOR OF THE BLOOD PLATELETS IN TOXEMIAS AND HÆMORRHAGIC DISEASE: A PRELIMINARY REPORT.*

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I desire to report in brief a review of thirty-one cases of hæmorrhagic disease studied with especial reference to the relationship between hæmorrhage and the platelet count; also clinical and experimental results which are thought to throw light on some of the factors causing pathologic fluctuation in the platelet count. In studying hæmorrhagic disease a means, described by the writer in a paper published elsewhere, called the bleeding time was used. The bleeding time denotes the duration in minutes of a hæmorrhage proceeding from a small cut in the lobe of the ear. It must not be confused with coagulation time—a term which denotes the rate at which blood clots.

Of the thirty-one cases studied, seventeen had normal or slightly increased platelet counts, fourteen had exceedingly low counts, below 65,000. (The normal count ranges from 200,000 to 400,000.) The group having the low counts differed clinically in many respects from the group having normal or increased counts—in fact the outspoken cases of the low platelet group presented a symptom complex simulated in its entirety by none of the cases having higher counts.

Discussion in this paper is confined to the low platelet group of cases. The severer of these were purpura hæmorrhagica, *i. e.*, purpura with hæmorrhage from one or more mucous membranes. The milder cases presented sometimes little or no purpura and little or no hæmorrhage from *normal* mucous membranes. Frequently the only evidence of hæmorrhagic diathesis was excessive hæmorrhage from some local condition; for example, bleeding from intestinal ulcers, bleeding varices in cirrhosis of the liver, profuse menstruation. One symptom constant in the severer cases and frequently present in the milder ones was a tendency to bleed from every abrasion of the skin. Some patients would bleed for hours from a mere scratch. In consequence of this tendency the bleeding time was greatly prolonged (twenty minutes to two hours). The prolonged bleeding time is thought to be the most characteristic symptom of the disease.

The platelet counts were enormously reduced in every case showing a bleeding time of ten minutes or more. In the milder cases it was below 65,000; in the severer cases below 10,000 and frequently below 1000.

A decrease in the platelet count has been considered characteristic of purpura hæmorrhagica by Denys, Hayem, Bensaude and others. My results show that the low counts are not confined to purpura hæmorrhagica, but are found also in cases of hæmorrhage due in part to local causes. I have also seen two cases of purpura hæmorrhagica in which the platelet count was normal. One of the cases was purpura hæmorrhagica associated with urticaria and intestinal crises (Henoch's purpura); the other was purpura hæmorrhagica in cholæmia. These cases had normal bleeding times and differed therefore in this respect from the cases with the low platelet counts.

Direct transfusion of blood was carried out in three cases. This procedure was followed by an immediate and complete relief of the hæmorrhagic diathesis lasting about three days. The bleeding time in one case was reduced from ninety minutes to three minutes, and in another from thirty minutes to three minutes. On the fourth day after transfusion hæmorrhage began again, and the bleeding times were again prolonged. The only striking change in the blood, to explain this period of relief, was the rise in the platelet count—evidently the direct result of transfusion. In two cases, where observations were made, the counts were 6,000 and 20,000 before transfusion, and 129,000 and 89,000 respectively directly after transfusion. The platelet counts decreased steadily after the first day, and on about the fourth day reached their previous low levels. Simultaneously with this decrease in number of the platelets the hæmorrhagic diathesis returned. There was no change in the coagulation time of the blood during the period in which the patients were observed. The period of relief was thought to be due directly to the presence of the blood platelets.

In one case of severe purpura hæmorrhagica, counts were made almost daily for a period of about four weeks. During this period the bleeding time was enormously prolonged whenever the count was below one thousand, and was shortened sometimes to ten minutes, when the count rose to about ten thousand. Where the count is at such a low level as this a slight rise seems to cause a noticeable amelioration of symptoms.

Where observations were made it was noted that the hæmorrhagic diathesis appeared simultaneously with the disappearance of the platelets, persisted as long as the platelet

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count remained extremely low and disappeared as soon as the platelet count rose. Occasionally the purpura cleared up or the hæmorrhage was less severe or stopped completely for a time during a period in which the platelet count was still low. A determination of the bleeding time, however, demonstrated that the improvement was apparent but not real, and that the patients were still bleeders.

Routine platelet counts were made on patients with diphtheria, nephritis, and phthisis. In this series the hæmorrhagic diathesis of the type described appeared in three cases. These were the only cases in which the platelet count was enormously reduced.

In a series of 41 experiments on animals, an effort was made to produce purpura hæmorrhagica experimentally by treating rabbits and dogs with benzol, tuberculin, and diphtheria toxin. These agents were chosen on account of the frequency of purpura hæmorrhagica in benzol poisoning, tuberculosis, and diphtheria. Severe purpura hæmorrhagica was produced in only one experiment. This was by the use of a sublethal dose of diphtheria toxin. In this animal, two weeks after the administration of the toxin, the platelet count, which had previously risen and reached a height of 1,700,000, suddenly fell so low that platelets could hardly be found in the counting chamber. On the day on which the platelets disappeared from the circulation petechiæ appeared on the ear, and the bleeding time, obtained from cutting the skin, was enormously prolonged. On the following day the animal's cage was spattered with blood. This condition, since there was a petechial rash, and a tendency to bleed from every abrasion, corresponded with the disease as seen in man. The hæmorrhagic period persisted three days and disappeared on the fourth. It was on this day that the platelet count rose. Neither purpura nor prolongation of the bleeding time was noticed in two other rabbits treated with the same dose of toxin, nor in six rabbits treated with a larger dose. In these animals the platelet count did not descend below the critical level.

Purpura hæmorrhagica conforming to the type described, has been observed by me complicating chronic ulcerative colitis, spastic constipation, tuberculosis, diphtheria and aplastic anæmia. Cases evidently of this type have been reported by Hayem and Bensaude in lymphocytic leukæmia, hæmorrhagic smallpox and tuberculosis, by Pratt in nephritis and by Selling in aplastic anæmia due to benzol poisoning.

The condition has been observed then complicating a variety of diseases and has been produced experimentally. The one feature in common was the reduced number of platelets. That there exists therefore a causal relationship between an absence of blood platelets and a certain form of hæmorrhagic diathesis seems highly probable. The disease includes most but not all cases of purpura hæmorrhagica, and in addition many cases of local bleeding.

In studying blood coagulation in this series it was found, as noted by Denys and Hayem in their cases, that the coagulation time was not delayed, in fact it was often even shorter than normal; also that fibrin was formed in abundance and had a normal microscopic appearance. It was seen further that in animals with severe benzol poisoning and a markedly reduced platelet count, the fibrinogen content of the blood was normal. As discovered by Hayem blood free from platelets, although it clots rapidly, does not retract from the sides of a vessel containing it and extrude serum. Whether this phenomenon is to be attributed to abnormal fibrin or whether it is due to the fact that platelets are not present to anchor together the filaments of fibrin, is not clear. Absence of retractility was found in this series of cases whenever there was a marked reduction in the platelet count.

In accounting for hæmorrhagic diathesis it is difficult to eliminate entirely certain possibilities which have been frequently suggested as a cause of purpura in this and other types of disease, namely: abnormal vessel walls, abnormal coagulation, capillary emboli, etc. It may be that such conditions play a contributory rôle in the pathogeny of this disease. The tendency to bleed, however, can be accounted for without assuming their presence, as follows: hæmorhage is not checked to any great extent by a clot such as is seen on the surface of a wound, but chiefly by an intravascular thrombus—a structure having an entirely different architecture and mode of formation. A clot formed from still blood consists of a homogeneous mixture of platelets, red cells, leucocytes, fibrin etc. A thrombus formed from flowing blood, on the other hand, as demonstrated by Hayem and others, has a totally different structure and is made up to a large extent of masses of agglutinated platelets. It has been repeatedly demonstrated that after injury to a vessel wall, platelets are the first element to adhere to the injured intima, and are deposited in enormous numbers before fibrin is laid down in demonstrable quantity. From the structure of the thrombus alone, it would be natural to expect that an absence of platelets would cause an abnormality in its formation or initiation, and would therefore be a cause of prolonged bleeding whether the fibrin-forming factors were normal or not. The fact that an individual may bleed for two hours from a pin prick, when platelets are absent, is sufficient evidence that thrombi do not form in this condition, and suggests therefore that the rôle played by platelets is an essential one.

The studies on hæmorrhagic disease brought to light facts thought to show a possible cause of pathologic variation in the platelet count. In the experimental work it was observed that the subcutaneous injection of large doses of diphtheria toxin (doses which proved fatal in three to four days) causes an immediate fall in the platelet count. Sublethal doses, on the other hand, cause an enormous rise followed by a fall, or simply a rise in the count. The same general rule applies to animals treated with benzol. The injection of large doses of benzol causes a rise in the count followed by a rapid fall, while the use of smaller doses causes a marked rise. The injection of tuberculin causes only a rise in the count, even when enormous doses are used. These experiments seem to show that a clinical pathologic variation in the platelet count is in many diseases the effect of a toxin on the platelet-forming elements (possibly also on the platelets in the blood stream). In large doses the toxin acts as a poison and in small doses as an irritant, or first as an irritant and then as a poison. Where the platelet irritant is a strong one (diphtheria toxin for example) the count is

almost as frequently increased as decreased. Where the irritant is mild (as in tuberculosis for example) the platelet count is usually increased, but in case of an unusually large dose or of a peculiarly susceptible individual it may be reduced. This hypothesis fits well with my counts in diphtheria and phthisis. In diphtheria I found the change observed by Hayem in many acute diseases, and called by him a "hæmatoblastic crisis," to be the rule; that is, the count was usually reduced (in one case to 3,000) during the febrile period of the disease, and increased during convalescence (highest count 750,000). The opposite change, however, was also observed; that is an increase in the count during the febrile period and a fall during convalescence. In advanced phthisis my figures show that the count was usually increased, sometimes enormously so (highest count 1,100,000). In two cases, however, it was enormously decreased for a short time, once below 1,000.

Summary.

To summarize, then, variation in the platelet count in many diseases is largely the effect of toxins, some of which in small doses increase the count and in large doses decrease it. When the count descends below a level of about sixty thousand there may be an abnormal tendency to bleed. When it descends below about ten thousand, this tendency is always present, and when below one thousand, is present in its most severe form.

In conclusion I wish to express my thanks to Dr. Hugh Cabot and Professors Murphy, Romberg and von Noorden for the privileges granted me in their clinics; to Dr. J. H. Wright for suggestions about methods for counting platelets; to Dr. G. H. Whipple for his kind assistance in making fibrinogen analyses and Dr. L. Selling for suggestions as to the use of benzol.

AN ALVEOLAR TUMOR OF THE CAROTID GLAND WITH SARCOMATOUS TRANSFORMATION.

By Paul G. Woolley, M. D., and Frank Fee, M. D.

(*From the Laboratories of the Cincinnati Hospital.*)

INTRODUCTION.

By Frank Fee, M. D.

Of recent years tumors of the carotid glands have been receiving more and more attention from surgeons, and cases appearing from time to time in surgical literature show that they are less rare than formerly supposed. These glands derive surgical importance from the fact that they are so closely related to the carotid arteries, the deep jugular vein and such important nerves as the sympathetic, hypoglossal, lingual and vagus. This intimate connection to the carotids necessitates ligation of these vessels in about 60 per cent of the cases. Then, too, any or all of the above-named nerves may be injured or completely severed during operation.

Tumors of this gland are not easily diagnosed, as shown by the early reports. They have been mistaken for enlarged lymphatic glands, lipomata and even goitre. In my own case, I had made a diagnosis of carcinoma of the lymph glands, following what I took to be a carcinoma of the thyroid gland. It was my intention, first, to remove this lymph gland, which caused the patient the greater discomfiture, and then should her condition warrant to remove the thyroid. The removal of this required one and one-half hours and I discontinued the operation after its removel. In this case I feel that I was extremely fortunate in not having to ligate the vessels or injure the nerves.

Keen admirably describes the diagnostic symptoms and signs as follows:

The diagnosis based on positive and negative facts. The Positive Facts: 1. There is a tumor arising in the region of the bifurcation of the carotid; that is to say, about on a level with the upper border of the sternocleidomastoid, but when it has reached any size it is only partly covered by this muscle. 2. The tumor is moderately movable horizontally, but not vertically. 3. It is usually ovoidal in shape. 4. As a rule it is smooth and not lobulated. 5. It is a singular tumor and not made up of a coalescence of several tumors, as in tuberculous glands. 6. There may be bruit and thrill, but this is rare and not marked. 7. There is transmitted but non-expansile pulsation. 8. It may cause bulging of the wall of the pharynx. 9. The pupil is occasionally contracted. 10. It will usually grow slowly at first, and possibly, shortly before the surgeon sees it, more or less rapidly. 11. It will have existed for a number of years. 12. The consistence is neither very hard, nor very soft, but elastic. The Negative Facts: 1. There is no pain. 2. As a rule it is not tender. 3. There is no disturbance, as a rule, of the pneumogastric, either as to its cardiac or laryngeal functions. 4. There is no disturbance of the sympathetic nerve. 5. There is no change in the pupil, except occasionally. 6. So far as the patient is concerned, there are usually no subjective symptoms, but the aid of the surgeon is sought on account of a slowly or rapidly growing deformity, and if the tumor is growing rapidly there may be also fear of its results.

My patient, Mrs. X., aged 68, was fairly well developed, but poorly nourished. She first noticed a goitre developing five years ago. She had consulted several physicians at various times, and had taken thyroid extract for periods of one month on several occasions. The tumor on the right side of the neck, independent of the goitre, made its appearance about two years ago, and had gradually grown larger.

Examination.—Pulse 110, respiration 20, temperature 99.6°F. Heart, lungs and kidneys negative. The pupils reacted to light and accommodation and were normal in size. The neck was considerably emaciated. The thyroid gland was

found to be enlarged on both sides, but more marked on the left where it was adherent to the trachea but not to the skin. The larynx was pushed well to the left side causing paroxysms of difficult breathing. Between the sternocleidomastoid muscle and the right lobe of the thyroid a mass about 2½ inches long and 1½ inches in diameter was found. Its shape was distinctly ovoid and its smooth capsule could be easily felt through the skin. With the patient lying on her back a distinct bruit could be heard, but upon turning face downward this disappeared. Pulsation could be easily felt, but was not expansile in character. Its consistency could be likened to that of an enlarged non-suppurating lymph gland. Its mobility was limited to horizontal movements, lateral motion being arrested by a small attachment to the thyroid gland.

Operation.—June 9, 1910. An incision was made over the most prominent portion of the tumor and its capsule exposed. With blunt dissection the internal and external carotid arteries were exposed and separated from the tumor. Ligation of these arteries was not necessary. Owing to the tedious character of the operation and the poor condition of the patient it was thought advisable not to attempt to remove the thyroid gland. Drainage was inserted in the lower angle of the wound which was closed with silk-worm gut.

Remarks.—The patient rallied from the operation and did fairly well for several days. A slight purulent discharge developed in the wound and later symptoms of a mild septicemia appeared following which the patient gradually grew worse until July 13, or 23 days after the operation, when she died.

A post-mortem examination was not made. The tumor was sent to Dr. Woolley for pathological diagnosis.

PATHOLOGIC REPORT.

By Paul G. Woolley.

Tumors of the carotid glands are not common. The reasons for this are probably two, though we know but one, and this is that the glands themselves are of inconstant occurrence. For example, Funke found carotid glands in but one of eight fœtuses, and Gomez found them in but five of fifty human bodies. In four of these only one gland was present. This inconstancy has been remarked by all observers from the time of Haller to the present.

The site of the carotid glands (*glomera carotica*) is the region of the bifurcation of the common carotid artery. In this region they are found, as a rule, situated posterior and mesial to the bifurcation so that they come to lie nearer to the internal carotid. They are supplied by a single nutrient artery from the arterial trunk nearest to which they lie, and they are connected to this trunk by a fibrous pedicle, called the ligament of Mayer, which is continuous with the capsule of the gland and the adventitia of the artery. In it the nutritional vessel runs, and passes into the gland, accompanied by numerous medullated and non-medullated nerve fibers, at the hilus. The capsule of the carotid bodies send numerous septa into the organ and divide it into the so-called "secondary nodules," each of which is divided into smaller cell masses commonly called the *Zellballen,* which are composed of the cells which are characteristic of the organ. These cells are large, rounded or polyhedral, have a clear protoplasm, and contain large, round, well-stained nuclei. They lie closely adjacent to the endothelial layer of the capillaries. This appearance is, as Mönckeberg says, best seen in the glands of young individuals, since with increasing age the fibrous tissue increases and separates the cells from the blood vessels. Marchand believed that these typical cells are derived from vascular loops. Paltauf also believed them of vascular origin, but rather from perithelium. Schraper could find no evidence of endothelial origin. Stilling observed chromaffin cells in the carotid bodies and hence came to the opinion that the glands are similar in origin to the adrenals. Kohn also, mainly upon the basis of the presence of chromaffin cells, sympathetic ganglion cells and the abundance of non-medullated fibers, thought that the *Zellballen* were composed of cells derived from sympathetic cells. But up to the present time there is no defined consensus of opinion as to the origin of these glands.

It is therefore impossible to refer to tumors arising in the carotid glands except in morphologic terms and to speak of them as Kaufmann does as "alveolar tumors," for until there is greater certainty regarding their origin it seems wiser not to use the term angiosarcoma, perithelioma, carcinoma, or endothelioma. According to Stieda, Rabl, du Meuron, Maurer, and others, the carotid glands are derived from the third or fourth branchial cleft. Katschenko, Paltauf and Szymonowicz, Marchand and Mönckeberg believed that they originate from the perithelium of the carotid arteries. Luschka and Kohn think them of sympathetic nervous system origin like the medulla of the adrenal.

The tumor, which serves as the basis of this report, measured 6.5 x 3 x 3 cm., and weighed 35 gm. It had the general shape and appearance of a small clean potato. It had been preserved in formalin. The surface was generally smooth and was modified by the appearance of flattened or rounded elevations which projected but slightly above the general surface of the tumor mass. At one point there was a teat-like projection that measured 2.5 x 1 cm. The general color was bluish-gray modified irregularly with yellowish patches, or mottled with brownish-red. The teat-like projection, which, like the main tumor, was lobulated, had a generally light yellowish-white color with smaller brownish mottlings. The whole mass of the tumor was enclosed by a smooth thin capsule from which five strands passed into the tissue between the lobules. Except for the resistance caused by these penetrating strands, the capsule could be readily removed. It was not adherent to the substance of the tumor except at a few places. At no place was there evidence of a direct penetration of the capsule by the tumor, though there were a few small dark lappets that seemed to perforate the thicker parts of the capsule, but these lappets also were covered by a very delicate membrane. Such projecting masses measured not more than 3 mm. in length. In consistence the tumor was for the most part firm, but at one pole it had a partially spongy or cystic feel. It was rather friable, and after removal of the capsule, especially from the

large teat-like process, could be separated partially into its lobules.

The color of the cut surface varied. At one pole (the upper) it was generally yellow, but with small grayish areas that were minutely cystic in appearance, and with other bluish hyaline zones surrounding the yellowish, more solidly cellular, areas. Practically one-third of the entire tumor had this structure. The central third was rather more generally mottled with yellowish-brownish-red and bluish hyalin, the latter apparently due to the presence of the homogeneous contents of small cystic spaces. The yellowish parts had a granular friable appearance. The lower third of the tumor mass was predominantly cystic, the individual spaces of which ranged from the size of a pin point to 3 mm. in diameter. In color this part was dark, reddish-brown or brown, and with more hyalin than the other parts of the tumor. Between the cysts the tissue was, as a rule, grayish and occasionally of a whitish homogeneous appearance like hyaline fibrous tissue. The teat-like mass was pale or yellowish and almost uniformly solid. It contained one large cyst with brownish-red hyaline contents, near the outer third, and a second small one, with almost black contents just at the base.

Bits of the tumor were taken from various parts, imbedded in celloidin and paraffin, cut, and stained with hematoxylin and eosin, iron hematoxylin, orcein-thionin, van Giesen and Mallory's aniline blue. The sections stained by the latter method were taken from tissue that had been treated with picric acid followed by ammonium bichromate.

Histologic Structure.

In a general way sections showed that the tumor was alveolar and cystic—as a matter of fact the predominating feature of the tissue was its exquisite alveolar arrangement.*

The larger cystic spaces were lined with a columnar or cuboidal epithelium that was regularly arranged and which occasionally showed a tendency to intracystic papillomatous overgrowth (Fig. 4). These lining cells showed an almost complete uniformity of structure; the nuclei were vesicular and were provided with deeply staining nucleoli, and surrounded by a reticulated protoplasm in which no extraneous substances were visible. An occasional cell showed enormous increase in size, which, with the rounded contour and accentuation of the reticulation and vacuolation, seemed to indicate an edematous degenerative condition. The contents of these cysts were composed of a hyaline, usually slightly acidophilic, clear, homogeneous, or partially granular material, in which were imbedded larger or smaller numbers of red blood corpuscles, polymorphonuclear and mononuclear leucocytes, and pigmented epithelioid cells. Certain of such cystic spaces were filled with blood. In others blood had very probably been present, but had been absorbed so completely that but little pigment remained, though the pericystic connective tissue, in the meshes of which pigment-carrying cells could be seen, were deeply stained. There was no sudden transition between these cystic structures and the following which approached in their appearance the follicles of the thyroid. These follicular structures were of two main sorts: one in which the most exquisite interacinous growth was discovered (Fig. 1), and one in which there was no such picture. In both the lining cells were cuboidal, sometimes flattened and as a rule one row in thickness. The contents of such structures had a hyaline or colloid appearance and this was, as a rule, clear and achromatic, or, occasionally, somewhat basophilic, staining blue with thionin, and hematoxylin. This material seemed to be, in at least some instances, the product of cell degeneration, for frequently one could see in it the faint shadows of cell outlines. In other instances no structure could be observed. In other areas this follicular structure was less in evidence because of the papillomatous overgrowth which was as characteristic and delicate as the interacinous growths of certain adenomas of the breast, and this was so accentuated at times that comparatively large areas were seen which were composed of rambling, interlacing columns of cells that produced secondary acini by their interweaving (Fig. 6). In some of these complexes the cells were of the typical high columnar type with the nuclei distal to the centers of the cells. The areas that were less cystic and less follicular and more glandular in character were characterized by appearances that were but accentuations of those described above. The general difference was that there was an increase in epithelial cells with no evident tendency to cyst formation or to intracystic or intra-acinous papillomatous overgrowth (Fig. 2). In such places the cells were arranged, sometimes in rounded or compressed masses with some or no evidence of a central space, sometimes in parallel columns several cells in thickness.

In none of the areas thus far described was evidence of malignancy encountered. The cell masses and columns were sharply limited by the supporting tissue and mitotic figures were found only in exceptional instances. As a matter of fact there was no evidence that growth has been anything other than slow. But there were certain parts of the tumor in which the line of demarkation between parenchyma of supporting tissue was indistinct and in which there was evidence of invasion—of infiltration (Fig. 3). In such areas there was less of an orderly arrangement of the cells. Cell columns were irregular and were composed of many layers of irregularly arranged cells in which mitotic figures were more frequent than in other parts of the tumor. In the region of the tumor where this atypical, more or less solid structure was found, there was also some cystic and even intracystic growth (Fig. 3). The walls of such cysts and the papillary growths were composed of several layers of cells—often many—but in these layers there was a lack of order. Moreover the cells varied enormously in size and shape. There were no columnar cells and few cuboidal. All or nearly all were polymorphous with large nuclei and with relatively less granular or spongy protoplasm. Again, whereas the parenchymatous cells were arranged in masses, as a rule, there were areas where they were scattered in the con-

* For the purposes of description, the tissue will be divided according to its gross microscopic structure, it being understood that all transitions occur between different general types of arrangement, and that this division is purely artificial.

Fig. 1.

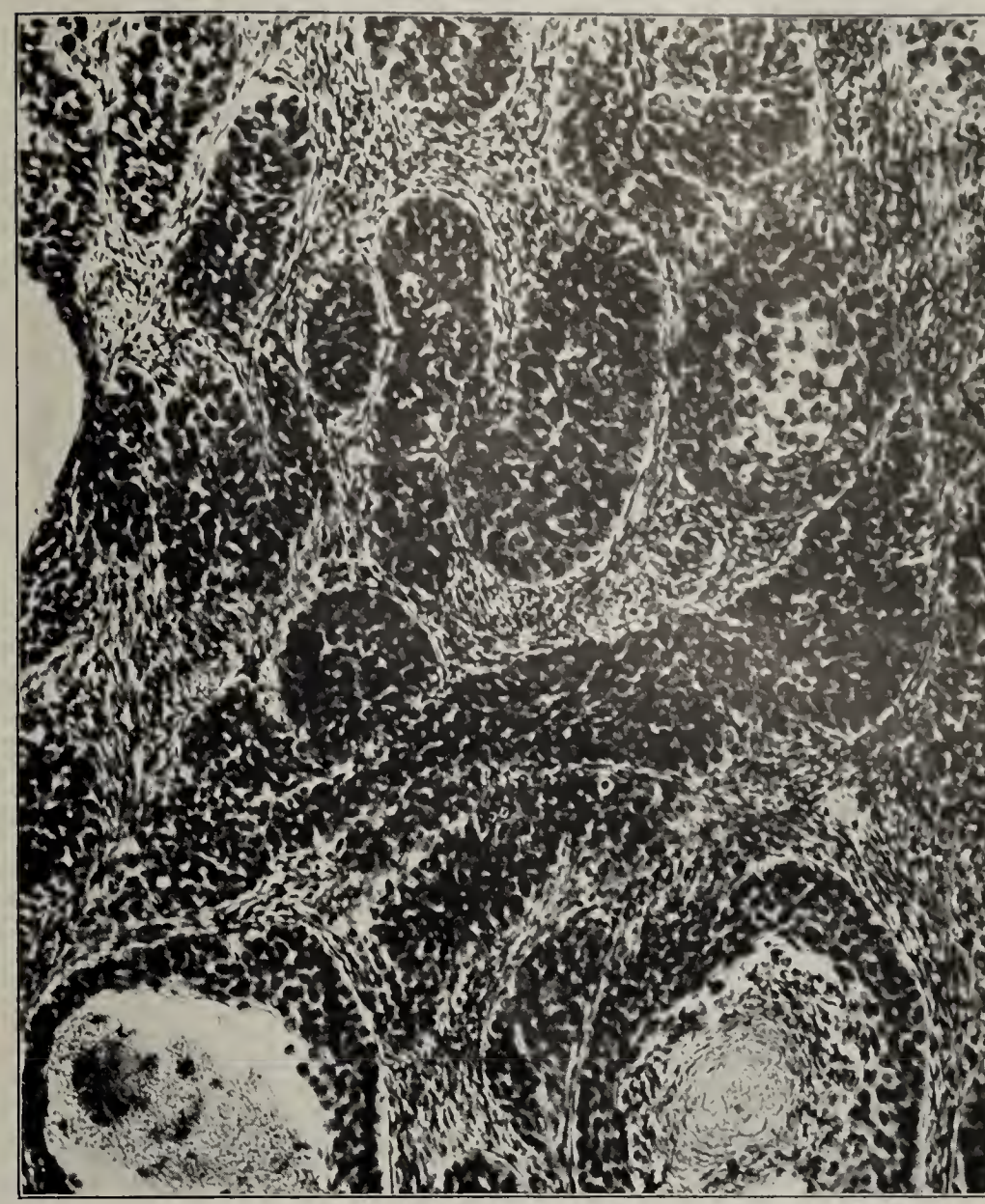

Fig. 3.

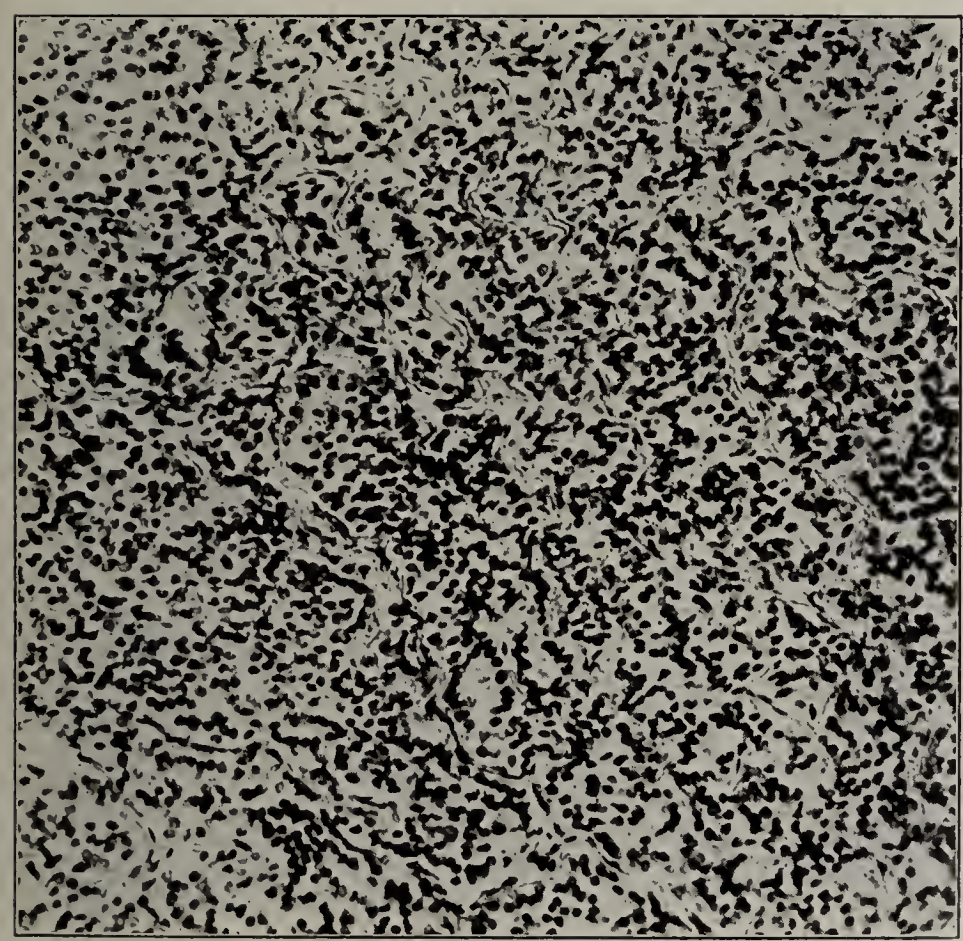

Fig. 2.

Fig. 4.

nective tissue, sometimes in irregular slender columns, but also in small groups, and even singly. There was the further interesting fact, also, that, in the region in which there was evidence of infiltration from the side of the parenchyma, there were also symptoms of increasing activity on the part of the connective tissue (Fig. 3). It was not merely hyperplastic, but unusually cellular, rich in ovoid and spindle-shaped nuclei and contained many mitotic figures. The fibers were more or less arranged in bundles, some of which were cut in cross, some in longitudinal section. There was a fairly abundant infiltration with small round cells.

Elsewhere the connective tissue was in only moderate amount; it had a generally healthy appearance, but also showed occasional hyaline areas.

The larger blood vessels showed but little change. In the purely follicular parts they were either normal in appearance or showed a moderate amount of hyalinization. In the malignant parts they showed a more widespread hyaline change.

It is difficult to estimate the relationship, if one exists between the small blood vessels and the tumor. There were areas in which there was a perivascular arrangement of cells, but this was never typical. There was no palisade formation, and the cells had none of the usual clear transparent appearance of the typical perithelium. The same was true of the malignant parts of the tumor, so that one is inclined to think that growth proceeded along the vessel sheaths, rather than that it originated in them. In these ambiguous locations there was always an apparently normal endothelial lining in the vessels. There was also no evidence at any place of an intercellular reticulum (Fig. 7), a fact that speaks neither for nor against endothelioma, since, as I have shown, a reticulum may or may not be present in such tumors, though the tendency is to the former condition. Yet there is evidence, though not of the best, that at least a part of the tumor may be of endothelial origin. In some suggestive places there were all transitions from hyperplastic endothelial cells through solid cellular masses of epitheliod cells to areas in which the central parts of such masses had undergone degeneration producing pseudocystic figures (Fig. 3), in which the central contents are evidently cellular detritus and in which cell shadows can still be seen. In some of these also there was evidence of deposition of lime salts from a bare lacking to deeply staining granulation.

Résumé of Microscopic Appearance.

I. The tumor showed an exquisite alveolar structure, with all transitions from large cystic structures, containing vestiges of hemorrhages, to solid cellular masses and strands.

II. In the larger cystic spaces the lining cells were columnar or cuboidal and of but one layer (as a rule) in thickness. There was typical intracystic proliferation.

III. In the more solidly cellular parts the cell masses often showed central degeneration giving rise to the appearance observed in cylindromas. In some places there was evidence of deposition of lime salts in the degenerated material.

IV. There was evidence of perivascular progression; some of perithelial proliferation and some of endothelial overgrowth.

V. The tumor, in general, had the characters of a benign growth, but there were areas in which there was distinct evidence of malignant change, both in the stroma and parenchyma.

The Cells of the Tumor.

In the foregoing description mention has been made of the fact that the more or less cystic spaces were lined with epithelium that showed all transitions between a high columnar and low cuboidal form, and that these cells, as a rule, were arranged in single rows. Occasional pigmented cells of two types were encountered—those that were phagocytic carrier cells, and those which were apparently not carrier cells. There were other cells that presented enormous variation in size, form, and microscopic appearance, both as regarded the general appearance and the nuclear structure. Such variations were present not only in the epithelial portion, but also in the stroma.

Certain changes have also been observed in the appearances of the vascular endothelial cells, and in the cells immediately associated with the blood vessels. It is with these appearances that the following paragraphs will be concerned:

According to various authors there are at least three types of parenchymatous cells in the carotid bodies. The predominant type is large, more or less irregular in form, but with the tendency to be cuboidal or polygonal. These cells have vesicular nuclei with distinct chromatin granules and a centrally placed nucleolus. Another type is one which has more or less of a lymphoid appearance. The protoplasm is relatively scant; the nucleus is round, deeply staining and contains chromatin granules. The third type of cell is the so-called chromaffin cell of Stilling.

Concerning the origin of these latter cells there seems to be no doubt. They are epithelial, derivatives, like those of the adrenal medulla, of sympathetic nerve cells.

On the other hand the origin of the predominating cells of the carotid bodies is in dispute. It is believed by some investigators that they are very closely associated with vascular endothelium—that they are in effect outgrowths of such a tissue. Others suppose that though they are derived from endothelium they have become independent to the same extent as the adrenal cortical cells. Upon either supposition tumors would be classified with the mesotheliomata, but in the first instance they would represent vascular tumors, *i. e.*, true endotheliomata; in the second they would be classified with the tumors, which, like those of the adrenal, have no evident vascular origin or arrangement. There seems to be no consensus of opinion on these taxonomic questions, though it is generally believed that the glands are of endothelial origin. If it can be shown that there is a definite relation between the alveolar portions of such tumors and the sarcomatous portions, then we shall have some evidence to support the view of the endothelial relationship of the cells. Such support will be derived in this way: True endotheliomas do not show a typical alveolar appearance such as is presented in carotid tumors, though it is true that they may show sarcomatoid variations. Tumors of

the adrenals, to use a single instance, may originally have an alveolar structure and appearance and may also, in the original growths, as well as in their metastases, show a structure that corresponds exactly with that shown by typical sarcomata. Examples of this have been published by Jores, Woolley and Meakins. If then it can be shown that there is a true transition from adenomatous (carcinomatoid) structure to sarcomatoid, we shall be in possession of evidence of mesothelial origin of the carotid gland.

The cells of the tumor under consideration are generally of the large cell type. They are polymorphous. The nuclei are large, oval, round or occasionally angular. They are more or less vesicular with a reticulated structure, the fibrils of which radiate from a distinct central chromatin granule or nucleolus to the peripheral chromatin-studded limiting membrane. The depth of staining reaction varies considerably, but the structure is generally the same in all the cells. Most of the nuclei show, beside a nucleolus, smaller chromatin granules. The protoplasm is, as a rule, relatively abundant and frequently achromatic, though usually and but moderately acidophilic. It is reticular in structure, and occasionally contains granules or droplets of a light or brownish-yellow material that resembles the lipoid granulations of other organs (Fig. 5). The form of these cells vary as already has been mentioned from high columnar, through low cuboidal, to polymorphous. The more columnar cells are relatively richer in protoplasm, and the nuclei tend to be oval. The angular nuclei are probably due to fixation. The size of these cells varies enormously, ranging from some as small as mononuclear leucocytes to others ten times as large. In such huge cells the nucleus and protoplasm are both increased, the gain in the latter being greater. The same general structure is preserved. No more cells of lymphoid type have been encountered than one could account for on the basis of an hematogenous origin.

It therefore appears that the alveolar portions of the tumors are composed of but one type of cell, that of which the primitive *Zellballen* are composed in the normal gland. The pigmented cells perhaps need explanation. The pigmentation appearances of some of these is evidently due to the remains of blood pigment. In others, such as are situated at considerable distance from areas of hemorrhages, this explanation is not so satisfactory. The suggestion occurs that these cells are related in a more or less direct fashion to the cortical cells of the adrenals. They do not show the characteristic color and appearance of chromaffin cells.

Concerning the relation of the cells of the alveolar portions of the tumor to the blood vessels there is little to be said. They were evidently, so far as our observations are concerned, entirely unrelated, directly at least, to the endothelium of the vessels. Even at points where there was the wheel or concentric arrangement, there was no evidence of endothelial origin, but rather of perithelial progression. Though the tumor was rich in small blood vessels and capillary networks there was no place at which a relation between tumors and endothelium seemed possible.

In many alveoli, especially in the malignant portions of the tumor, there was a gross morphologic appearance that suggested endothelioma. Here the alveoli were often lined with one or many rows of flattened cells about a central hyaline or bluish laked or granular mass which was due to central alveolar degeneration. The appearance produced was that encountered in cylindromas. Such central masses were evidently composed of degenerated cells, for shadows of cells and nuclei could be seen with the proper powers of the microscope. Around such alveoli the capillaries appeared healthy. It was in such localities that the greatest variation in the size of the cells was observed. Syncytial formations also occurred.

At points where infiltration was in evidence, there was less variation in the size of the cells. At such places the columns or single rows of cells and isolated epithelial cells were of generally uniform appearance. They were rather more spindle-shaped than the alveolar cells, but evidently not of the sarcoma type. The stroma in which they were imbedded had, however, undergone malignant change and was composed of spindle cells of a rather slender variety. It was infiltrated with small round cells and a considerable number of polymorphonuclear leucocytes.

In résumé we may say: (1) The cells of the alveolar parts of the tumor and of the stroma were apparently autonomous, though both exhibit malignant changes, and neither had any apparent close or definite relation to the endothelium of the blood vessels.

(2) That the cells of the alveolar portion were of one main type and corresponded in general appearance with the large cells of the original *Zellballen*. The proliferated and infiltrating stroma cells were of the spindle cell variety.

(3) The changes in the blood vessels seemed to be relatively unimportant. There were very occasional places where there seemed to be some localized hyperplasia with a tendency to the production of polypi composed of cell masses with no evidence of cell boundaries (syncytium). This process seemed to have no particular connection or relation with the other changes in the tumor.

We believe that but two other tumors of this sort (*i. e.*, showing definite sarcomatous change) have been reported; that of Leithoff, and that of Kaufmann and Ruppaner.

BIBLIOGRAPHY.

Many references mentioned in the text have been consulted, but there seems to be no need to extend the bibliography by merely repeating references given in other works. Therefore, only what seem to be the most complete and modern articles are cited here.

Kaufmann and Ruppaner: Deutsche Ztschr. f. Chir., 1905, LXXX, 259. (Contains a complete review of the literature.)

Mönckeberg: Ziegler's Beiträge, 1905, XXXVIII, 1.

Gomez: Am. J. M. Sc., 1908, CXXXVI, 98.

Keen and Funke: J. Am. M. Ass., 1906, XLVII, 469 and 566.

The questions relating to the structure and development of mesotheliomas are discussed in a complete and comprehensive way by Adami in his Principles of Pathology, 1910, Vol. 1. In this volume the work of Jores, Woolley, Meakins and others is cited and the references given (pp. 677 and 706).

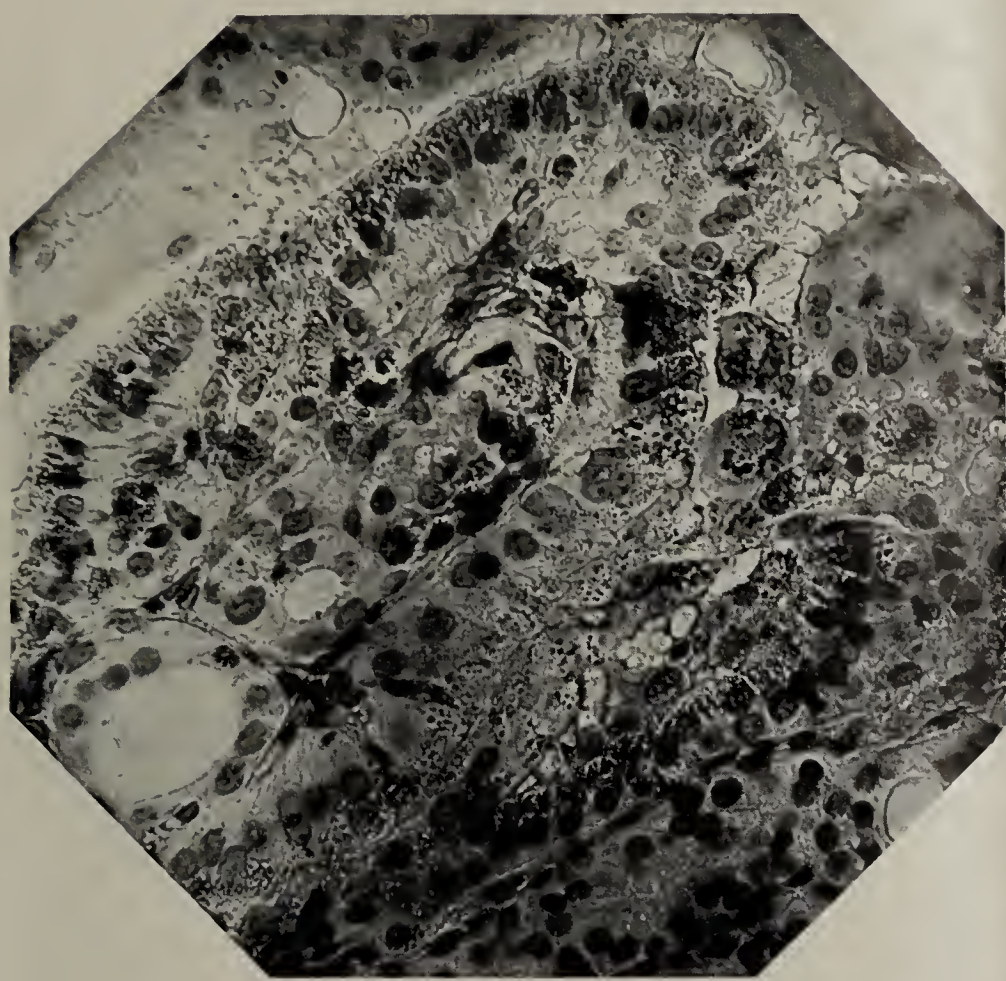

Fig. 5.

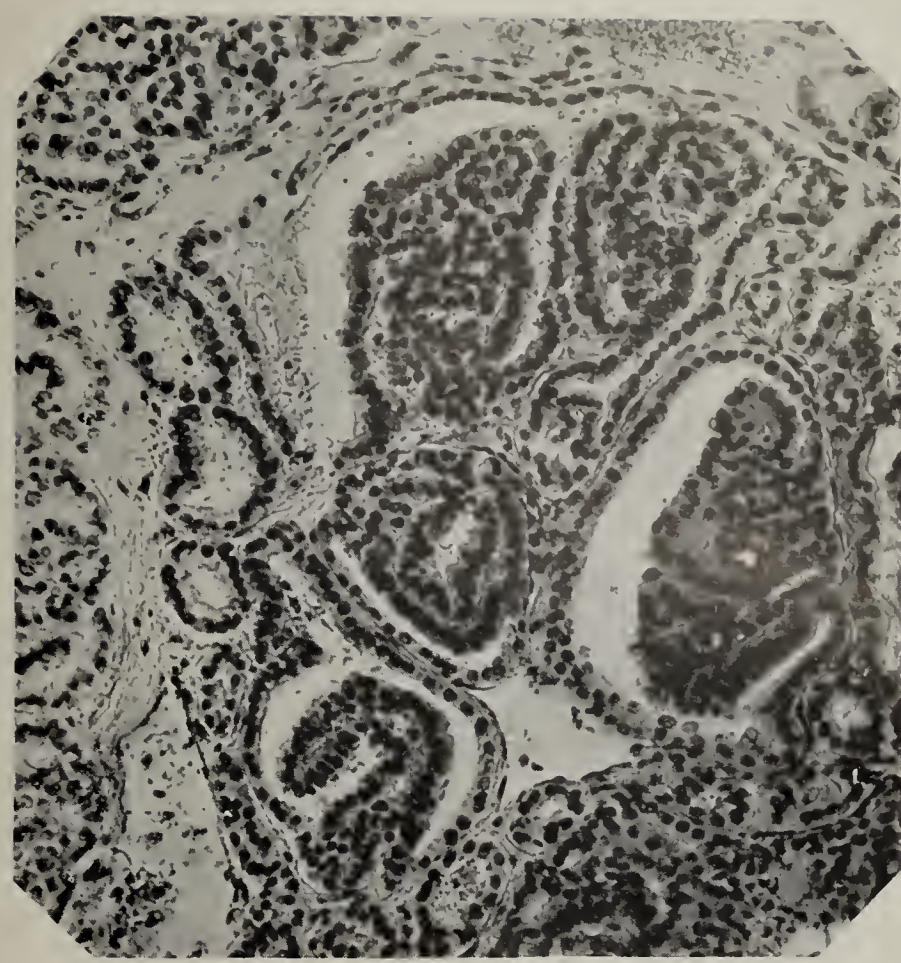

Fig. 6.

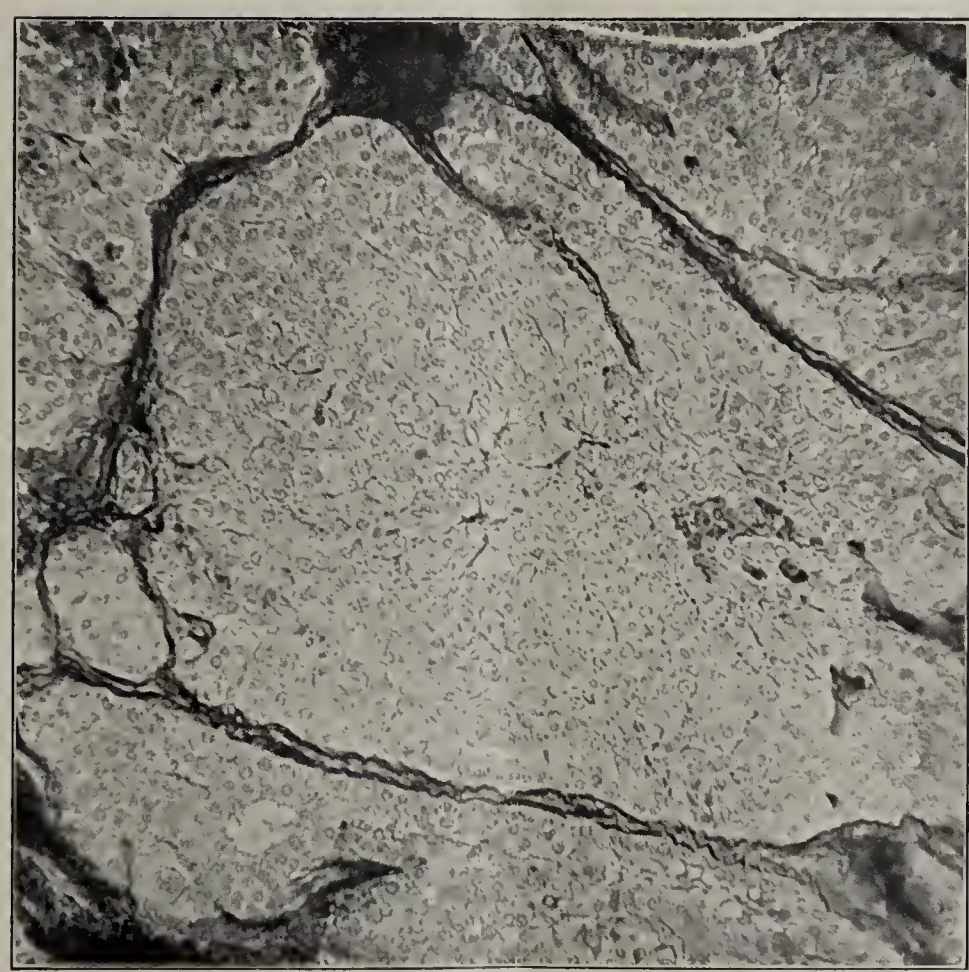

Fig. 7.

ILLUSTRATIONS.

(Photomicrographs by Dr. Charles Goosmann.)

Fig. 1. Section of the tumor showing the delicate intracystic papillomatous structure of certain parts.

Fig. 2. Section showing the almost solidly adenomatous structure of certain parts.

Fig. 3. Section showing pseudocystic spaces, and evidences of malignancy in parenchyma and stroma.

Fig. 4. Section showing canalicular, cystic and intracystic growth.

Fig. 5. Section showing the structure of certain parts of the tumor in which the cells contain a lipoid-like (?) pigment.

Fig. 6. Section showing an accentuation of the appearance shown in Fig. 4.

Fig. 7. Section of the more solid portion of the tumor showing the arrangement of the reticulum.

NOTES ON NEW BOOKS.

Emergency Medical and Surgical Aid. A Manual of First Aid for Laymen, with Special Reference to Industrial Accidents. By Ernest A. Wells, M. D. (*Hartford, Conn.: Published by Ætna Life Insurance Company.*)

Any person who will make himself master of the directions given by Dr. Wells in this well arranged handbook will, when the emergency arises, be able to give useful assistance. There are however in the author's directions several points to which exception may be taken. Under "Drowning" he states that there is no possibility of resuscitation if the patient has been completely submerged for seven or eight minutes. As it can hardly ever be known how long the patient has been completely submerged, efforts at resuscitation should be prolonged for as much as an hour or more.

Again under "Freezing" the writer says: "Gradually thaw out the frozen parts with warm water and rubbing. The tradition that you must use snow or ice water is absurd." The tradition may be absurd from one point of view, but is sensible, as there is little doubt that if warm water is used, it will be used too hot, and the frozen parts will be burned, as the patient has no feeling in the affected portion and so is unable to measure the heat of the water.

Under "Fits" Dr. Wells says the patient "may bite his tongue, it will do no harm and you cannot help it. Do not try to pry his mouth open, for you may break his teeth, and there is no sense in it." This advice does not recommend itself to the reviewer, who feels that efforts should be made to prevent the patient severely biting his tongue, of course without using so much strength as to break the teeth.

The outfit for a first aid is more suited to a doctor's office than to a layman's, but in large industrial institutions it would be wise to fit up a room with this stock.

It is a pity that the title page and the title on the cover do not correspond, and in a second edition the text will require some revision to perfect the English.

Serum Diagnosis of Syphilis and the Butyric Acid Test for Syphilis. By Hideyo Noguchi, M. D., etc. Illustrated. Second Edition. $2.50. (*Philadelphia: J. B. Lippincott Company, 1911.*)

The second edition of Noguchi's well known work upon serum diagnosis shows important revisions and additions to the first edition and will be welcomed by all those interested in serological methods and their application to clinical medicine.

One of the most valuable additions to the present volume is the chapter on the effect of treatment upon the serum reaction, which also discusses in some detail the results after treatment with "606." This chapter is one of great interest and importance to both the laboratory worker and the practising physician.

The essential facts of hemolysis and complement fixation are explained with simplicity and clearness. Too much stress, perhaps, is laid upon the author's modification of Wassermann's original reaction, and parts of the book give the impression that it was written as much for the purpose of advancing the author's views, as for presenting the general subject of serum diagnosis. This tendency is apt to give the beginner an undue preference for the author's own modification. To those familiar with both sides of the question, however, this presentation of the author's views is of great interest and quite stimulating, even if not wholly accepted.

The glossary at the end of the book is of great aid to those who are not familiar with the terms used in serum work. The statement, however, that complement fixation is synonymous with complement deviation, a term introduced by Neisser, is inaccurate or at least requires further explanation.

The bibliography is unusually complete and of great aid to the reader who wishes to consult original sources and go deeper into the subject. The book is well written, full of valuable data and statistics and can be heartily recommended to all those interested in the subject of serum diagnosis. R. H. M.

International Clinics. Edited by Henry W. Cattell, M. D., and collaborators. Vol. I. Twenty-second Series. $2.00. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

The paper of most interest in this volume is Flexner's on "Experimental Poliomyelitis," but others by Walsh on "The Masks of Diabetes" (much better than its title might indicate), Taylor's "Venereal Diseases in the United States Navy," and articles by Hill, Parke Weber, Kopetzky and Brooks will find many readers. We select a few names simply to indicate the varied nature of the papers rather than any special preference, for the internist, the surgeon, and general practitioner will each find something to hold his attention.

The Surgical Clinics of John B. Murphy, M. D., at Mercy Hospital, Chicago. Vol. I. Number I. Octavo of 133 pages, illustrated. Published Bi-Monthly. Price per year: Paper, $8.00. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

These "Clinics" have been recorded by a stenographer at the time the patients were operated upon by Dr. Murphy, and his talks are presented verbatim. This is a new venture both on the part of the author and the publishers, and one that cannot be commended for general adoption. Such informal talks may give one a good picture of the lecturer, and at times be entertaining and instructive reading, but they lack system, and the very method of their presentation is not attractive in book form. A lecturer must often repeat himself in an informal talk to doctors or students, but in his permanent writings he should show more style and finish. It is difficult to believe that these "Clinics" can prove of any real service to the profession, except as a record of Dr. Murphy's agreeable personality and his ability as a surgical teacher. Many will value them as we all like to preserve the spoken words of our friends, but they are two diverse and disjointed to serve for thorough teaching, which, after all, must be the real end to be aimed at in a series of clinics.

Kursus der Normalen Histologie. Ein Leitfaden für den praktischen Unterricht in der Histologie und Microscopischen Anatomie. Von Rudolf Krause, A. O. Professor der Anatomie an der Universität, Berlin. Illustrirt. Mk. 22.50. (*Berlin und Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

This very attractive manual is evidently intended as a guide for those who give courses in histology as well as for the student. The author has a short talk with the instructor in the introduction, in which he protests against the prevalent neglect of technical procedures in histological courses, allowing the student to depend upon his courses in pathological anatomy or even clinical medicine for a working knowledge of this subject.

The first hundred pages are devoted to a fairly thorough description of the various technical methods used in the study of histology. The remainder of the book, some 430 pages, contains 208 beautiful colored illustrations made from original drawings by the author. The text consists almost entirely of explanations or demonstrations of the figures which are numbered and carefully labelled. Each paragraph is headed by its appropriate title, the magnification of the specimen and the technique employed in its preparation with references to the first part of the book where the methods are described. The illustrations are excellent, and well chosen, the descriptions clear and concise.

This book will doubtless be a great boon to that great class of students who wish detailed and thorough demonstrations. Students of a different sort will find it convenient in verifying or correcting their own independent observations. It will be useful to all as a reference handbook of up-to-date technique.

Honan's Handbook to Medical Europe. A Ready Reference Book to the Universities, Hospitals, Clinics, Laboratories and General Medical Work of the Principal Cities of Europe. By James Henry Honan, M. D., etc. With Maps of Berlin, Edinburgh, London and Paris. $1.50. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This handbook is exactly what it is stated to be in the title, and Dr. Honan has compiled in excellent form a large amount of most useful information for students and doctors who intend going abroad for study or simply to visit some of the foreign clinics. This manual will prove itself invaluable to such travellers for the author gives data about 17 university cities in Germany, 6 in Switzerland, 6 in Great Britain, and others in France, Austria, Sweden, Denmark, Norway, Roumania, Greece, Belgium, Italy, Russia, Spain and Holland. With this book as a guide, medical travelers will find their way about much more easily in these centers, and Dr. Honan will, we are sure, have both the sincere silent and expressed thanks of many of his confreres for his work.

Second Review of Some of the Recent Advances in Tropical Medicine, Hygiene and Tropical Veterinary Science. Being a Supplement to the Fourth Report of the Wellcome Tropical Research Laboratories at the Garden Memorial College, Khartoum. By Alfred Balfour, M. D., Director, and Captain R. G. Archibald, M. B., in collaboration with Captain W. B. Fry, M. R. C. S., and Captain W. R. O'Farrell, L. R. C. P. $3.75. (*Published for Department of Education, Sudan Government, Khartoum. London: Baillière, Tindall & Cox, 1911.*)

All students of tropical diseases should be most grateful to the authors of this work. Here they can quickly find references to all the latest and best articles on practically every variety of disease occurring in the tropics. The reviews are well prepared and the number of articles that have been read and digested is enormous. While no such book can be complete yet it is likely that very few papers of importance have been overlooked, and it is to be hoped that the Wellcome Laboratories will continue to publish these Reviews. Medical literature grows apace and it is absolutely requisite for the student to have such books to assist him, as without them he would be quite lost in the mass of papers to be looked up on any tropical disease. In view of the size and handsome appearance of the book its price is cheap.

Minor Surgery. By Leonard A. Bidwell, F. R. C. S. Illustrated. (*London: University of London Press, 1911.*)

The author aims to give simple directions for the management of everyday minor surgical work, and in addition he has added very brief descriptions of certain major operations. Important points are emphasized by being printed in heavier type.

The book is similar to a number of others already on the market and offers very little, if any, additional information.

J. S. D.

Manual of Physiology for Students and Practitioners. By H. Willoughby Lyle, M. D., etc. Illustrated. $4.00. (*London: Henry Frowde, and Hodder & Stoughton, 1911.*)

A compressed text with few illustrations by an Examiner in Physiology appearing in its first edition. So far as it attempts to present the subject the book is open to little criticism. But the author's self-defined limits necessarily makes the book didactic, and therefore, lacking in inspiration to the student. Those interested in the science of physiology and the further introduction of this science into all medical work cannot but regret such a publication, however much it may supply the demands of students preparing for licensing examinations, since knowledge gained therefrom will scarcely stimulate effort towards the solution of problems either in the laboratory or clinic.

Progressive Medicine. Edited by Hobart Amory Hare, M. D., Assisted by Leighton F. Appleman, M. D. Vol. I, March 1912. (*Philadelphia and New York: Lea & Febiger, 1912.*)

The reviews of current literature in this volume cover the Surgery of the Head, Neck, and Thorax, Infectious Diseases Including Acute Rheumatism, Croupous Pneumonia, and Influenza. Diseases of Children, Rhinology and Laryngology, and Otology. A perusal of these chapters will keep a practitioner well informed as to the modern trend of view in regard to the diagnosis, treatment, etc., of these various diseases. The work is a useful addition to most doctors' libraries.

The Mechanism of the Heart Beat, with Especial Reference to its Clinical Pathology. By Thomas Lewis, M. D., M. R. C. P., D. Sc., Lecturer in Cardiac Pathology, University College Hospital Medical School, Physician to Out-Patients, City of London Hospital for Diseases of the Chest. 295 pp., 213 figures, 5 plates. (*London and New York: Paul B. Hoeber, 1911.*)

This book gives a very complete summary of the present day knowledge of the origin and course of the cardiac impulse under normal and abnormal conditions, particularly in the disturbances of cardiac rhythm. It is practically a collection and systematic presentation of the author's own studies with the electrocardiograph under normal and pathological conditions both clinical and experimental, and these have been sufficiently extensive to furnish material for such a monograph. Dr. Lewis' most important contribution to cardiac physiology has been the demonstration that the auricular (P) wave of the normal electrocardiogram indicates that the impulse for the auricular systole arises in the vicinity of the superior veno-auricular junction at the site of the sino-auricular bundle of Wenckebach and the node which had been described by Keith and Flack. His proof consists in the fact that extrasystoles from stimulation of this region give a P wave of normal form, while those arising from stimulation of other regions

in either auricle have an abnormal form, often a complete inversion of the P wave. He is thus able to differentiate in clinical cases between these two different forms of auricular extrasystoles, the "homogenetic" arising at the node of Keith and Flack, and the "heterogenetic" arising at some abnormal site; and he has found that many disturbances of cardiac rhythm in man, such as extrasystolic arhythmias and paroxysmal tachycardia, are due to the occurrence of such heterogenetic impulses.

Dr. Lewis gives an excellent discussion of the nature of the absolute arhythmia (formerly termed nodal rhythm by Mackenzie, arhythmia perpetua by Gerhardt, and pulsus irregularis perpetuus by Hering). In this field he has rendered excellent service by confirming the suggestion of Cushny and Edmunds and the electrocardiographic demonstrations of Rothberger and Winterberg, showing that the disturbance of rhythm is brought about by fibrillary contractions of the auricles which send impulses down to the ventricles at varying intervals. The material of over one hundred cases under the author's observation is carefully analyzed, and the frequency of mitral stenosis as a predisposing factor is shown. It is in this form of arhythmia that digitalis is especially useful, acting by preventing some of the impulses from reaching the ventricles. Dr. Lewis gives an excellent chapter on Adams-Stokes Disease and another upon the action of the vagus.

Paroxysmal tachycardia he regards as due entirely to coördinated heterogenetic impulses arising in auricles whose irritability is increased; but believes that a regular tachycardia is never produced by fibrillation of the auricles, though admitting that the latter condition represents merely a grade of irritability higher than that seen in heterogenetic tachycardia. The latter fact was shown by the reviewer in 1908 but the author does not refer to this earlier work. (Several cases of paroxysmal tachycardia with jugular pulse of the ventricular type, reported from Dr. Lewis' clinic since the appearance of the book, show absence of the auricular P wave and present some similarity to auricular fibrallation, so that the question as to whether auricular fibrillation always brings about an irregular pulse as claimed by Dr. Lewis or whether it may in some cases give rise to this type of tachycardia as suggested by the reviewer, seems still an open one.) Not the least of Dr. Lewis' contributions is the demonstration that paroxysmal tachycardia can be produced in animals by ligation of a coronary artery as well as it can be by faradization of the auricles or by the administration of drugs.

The book is beautifully illustrated with original electrocardiograms and ordinary graphic records obtained from both clinical cases and laboratory experiments and a number of good diagrams and there are unusually good figures of the sino-auricular node and auriculoventricular bundle.

The style is clear and the self-confidence which is so common to British writers tends to brush aside everything that is ambiguous and to contribute much to its readable quality. Nevertheless, the reader should not be blinded to the fact that many theories though dogmatically expressed by the best of investigators may lead but a transitory existence. The bibliography though not complete is adequate for the treatment of the subject matter in hand. All in all the book is certainly the most complete treatise in existence upon the phase of cardiac pathology with which it deals and we can warmly recommend it to all who desire to acquaint themselves with the physiology and pathology of the normal and irregular heart. A. D. Hirschfelder.

Practical Anatomy. The Student's Dissecting Manual. By F. G. Parsons, F. R. C. S. Eng., etc., and William Wright, F. R. C. S. Eng., etc. In Two Volumes. $2.40. (*New York: Longmans, Green & Co.; London: Edward Arnold, 1912.*)

There is no small type used in these volumes because unimportant details have been omitted, and "because in our experience" as the authors state in their preface "students usually pay more attention to the minutiæ contained in it [small type] than they do to the essential facts embodied in the large print." If this is true the English student must differ very essentially from other students. Every professor of anatomy must decide for himself what the unimportant details are, or what anatomical facts may be omitted from a student's text book on this subject, but we feel sure that it is rather the method of teaching anatomy which is at fault, than the extent and difficulty of the subject which explains the ignorance of most students when they are examined in anatomy. To write a book to make anatomy easy is a hopeless task and any comparatively brief work like this one can hardly give the student a thorough grasp of the subject. Gray's Anatomy in English still reigns supreme, and as this work has been constantly brought up-to-date, the student who has fifteen months to give to anatomy as in the English schools can afford a more comprehensive work than Parson and Wright's, many of whose illustrations seem to us only fairly satisfactory.

A Cyclopedia of American Medical Biography. Comprising the Lives of Eminent Deceased Physicians and Surgeons from 1610 to 1910. By Howard A. Kelly, M. D. Illustrated with portraits. Two volumes. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

The indebtedness of the medical profession to Dr. Kelly is great for his unselfish efforts to perpetuate the lives and labors of upwards of twelve hundred medical men of more or less eminence who have lived and labored in America during the past three centuries.

The biographies are short and concise and content themselves for the most part with furnishing the material facts of the life and history of physicians deemed worthy of mention. Now and then a strain of overwrought eulogy may be noted which suggests that a rhetorical flower may have been plucked from the tributes placed by fond friends upon the grave of some much-beloved physician. This, however, is rare. The biographies are especially written for the work or compiled from original sources and the thick volumes constitute a reliable and accurate store-house of facts. The author's purpose has been to give a brief outline of every medical man who has been distinguished as a "thinker, writer, teacher or leader." The biographies are generally models of good taste and the names have been judiciously chosen. Some omissions are to be noted and doubtless some differences of opinion will always develop among those who select names worthy to be included in such a cyclopedia. There is always a tendency in works of this character to record the deeds of the surgeon or brilliant specialist and to pass over those of the no less skillful and scientific general practitioner which may be less pyrotechnic in character and do not lend themselves to history. In the books before us the proportion of physicians as compared with surgeons and specialists is about three-fifths to two-fifths. It is interesting to observe that the great majority of the latter are the product of the last century. There was a time when the general medical practitioner was also a surgeon and possibly a dentist or an eye specialist. Nathan Smith, who founded four medical schools and filled most of the chairs in several of them, treated typhoid fever successfully by the original and novel method of cold bathing; he was also a bold and fearless surgeon and in addition operated for cataract whenever occasion presented itself. We notice the omission of the names of N. S. Davis, of Chicago, the founder of the American Medical Association, of Eli Todd, of Hartford, who was a mighty force in the development of public sentiment towards building institutions for the insane, of Henry J. Bigelow, of Boston, of Henry B. Sands, of New York, and others.

The cyclopedia is in marked contrast to the ambitious work of Gross which consisted of a few biographies given with much detail, the more concise work of Atkinson or the journalistic commercialized effort of Stone to constitute every man his own biographer.

Here the biographies have been edited with evident care and much literary acumen. The full bibliographies appended to each biography is an excellent feature.

The preliminary essays nine in number by Bardeen, Tinker, Alleman, Kelly, Winfield, Friedenwald, Delavan, Withington and Shasted are of unequal value but several are of great interest. They relate to "Anatomy," "Surgery," "Gynecology and Obstetrics," "Dermatology," "Ophthalmology," "Laryngology," "Women in Medicine" and "Medical Jurisprudence." The reader can but wish that similar essays on "Medicine," "Pathology," "Physiology" and "Psychiatry" had been added as of more general interest and importance than several which have been presented.

These suggestions, however, are minor criticisms and do not detract from the preeminent value of the book which deserves a large sale. The illustrations are excellent and the letter-press is attractive.

A Manual of Surgical Treatment. By Sir W. Watson Cheyne, Bart., F. R. C. S., F. R. S., etc., and F. R. Burghard, M. S. (Lond.), F. R. C. S., etc. New (2d) edition. Thoroughly revised and largely rewritten. In five volumes, containing about 3000 pages and illustrated with about 900 engravings. $6.00 per volume. (*Philadelphia and New York: Lea & Febiger, 1912.*)

This system of surgery, for it may well be called so in spite of the title, is the third large system in English which has appeared within a short time, and the smaller surgeries that have been printed in the last year or two are innumerable, not to mention all the works in special branches of this art, so that it becomes more and more difficult to recommend any one book to a student or practitioner of limited means. In these days of rush also few have time to thoroughly digest all the good mental food that is offered them, and it is in a sense to be regretted that the publishers are so active. It is, however, a pleasure to see a good old book reprinted, and, therefore, the profession is to be congratulated on the republication of Sir Watson Cheyne's manual, whose merits have well recognized. No real student of surgery can fail to want to know what surgeons in other countries than his own are doing and thinking, and the careful reader of this work will acquire new ideas and so become a better operator. The first volume is divided into five parts: (1) Inflammation and its Sequelæ; (2) Wounds and Their Complications; (3) Syphilis and Tuberculosis; (4) Tumors; (5) Deformities and an Appendix of two chapters on Anæsthetics and The Examination of the Blood in Surgical Conditions. Volume II is arranged in three divisions: (1) The Surgical Affections of the Soft Tissues, divided into thirteen chapters dealing with affections of the skin and subcutaneous tissues, of the nails, of the lymphatic vessels and glands, of fasciæ, bursæ, muscles, tendon sheaths, tendons, nerves, veins, arteries and aneurisms; (2) The Surgical Affections of the Bones in fourteen chapters beginning with one on General Considerations, followed by others on fractures of clavicle and scapula, humerus, forearm and hand, pelvis, femur, patella, leg and foot, acute and chronic inflammation of bones, necrosis and phosphorus necrosis, tuberculosis and actinomycosis, syphilitic and rheumatic affections, rickets and scurvy rickets, disorders of ossification, and tumors of bones; and (3) Amputations in three chapters of General Considerations and amputations of the upper and lower extremity. There is a great deal of ground, and many most important topics dealt with in this volume, and some of the chapters are brief, but on the whole the proportion of the different subjects is well maintained. The illustrations, though not brilliant, are sufficiently clear to demonstrate what is intended. Both volumes are indexed. Although the volume is too heavy, yet the publishers are to be thanked for not having made this manual so unnecessarily clumsy, as are the American systems, whose large volumes are an abomination. This system will long hold a prominent position among works on surgery by English writers, serving as a safe and clear guide to the young surgeon.

The Surgery of Oral Diseases and Malformations. Their Diagnosis and Treatment. By George Van Ingen Brown, D. D. S., M. D., etc. Illustrated. $6.00. (*Philadelphia and New York: Lea & Febiger, 1912.*)

As the gynecologists no longer confine themselves to the surgery of the female pelvic organs, but reach out to the kidney, gallbladder, etc., so the dentists are now reaching out from the teeth, and to them the medical profession owes already marked advance in the treatment of fractured jaws. Here we have a surgery on all oral diseases by a dentist, as well as a surgeon, a happy combination, and one which gives the book a distinctive character of its own. The author discusses pathological dentition, infectious diseases, diseases of the mucous membrane of the mouth, of the nervous system affecting the buccal region, of bone, of glands, tumors, diseases of the maxillary sinus, diseases, tumors and malformations of the tongue, nasal deformities and diseases in relation to the maxillæ, diseases, injuries and malformations of the lips, and harelip, cleft-palate, and defects of speech. The work is an extensive one and well illustrated with a few color prints. We might wish that so many surgeons did not feel it incumbent on them to introduce their works with a chapter on anæsthesia. The subject is too broadly handled by the author to be of real value, and this we feel to be the characteristic of his work. Had he not attempted to cover so much ground or had he gone more into detail in some parts, the book would have been better. As it stands however it will fill a want and prove very serviceable to a large body of students. The internist as well as the surgeon can get many good hints from it as to obscure conditions involving the mouth.

National Association for the Study and Education of Exceptional Children. Proceedings of the Second Annual Conference, 1911.

The care of the exceptional or backward child is certainly one of the most important problems that we have to deal with and social workers interested in the moral welfare of these children, who are often degenerates, will find helpful suggestions in the various papers here presented and classified under three headings: (1) Causes of Exceptional Development in Children; (2) Educational Needs of the Various Kinds of Exceptional Children; and (3) The Exceptional Child as a Social Problem. This is not a problem by itself but closely woven into other social problems, such as syphilis, alcoholism, tuberculosis, poverty, etc., so that the exceptional child can and should be studied from many different points of view. As good English this is a most unfortunate use of the word "exceptional" and the society should we think alter its name.

Die Methoden der Untersuchung des Magens und Ihre Diagnostische Verwertung. Von Dr. Emil Schütz, Privatdozent an der Universität Wien. $2.75. (*Berlin und Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

This is not simply a work dealing with the methods of gastric examinations but also a guide to the use of these methods in the differential diagnosis of diseases of the stomach. The author classifies his subject under the following headings: (1) Anamnesis; (2) The physical methods of gastric examinations; (3) Securing and examining the gastric contents; (4) Examination of the gastric contents without use of the stomach tube; (5) Examination of the functions of the stomach; and (6) X-ray examination of the stomach. He adds two chapters on the importance of blood and urine examinations in the diagnosis of diseases of the stomach, and one on the biologic methods to be

applied in the diagnosis of carcinoma. Dr. Schütz discusses not alone the application and use of older and newer methods but what makes the monograph valuable, he gives the result of his 30 years personal experiences with these. He lays especial stress on the estimation of the hydrochloric acid of the stomach and thinks that in spite of the doubt that some authors have expressed recently as to the value of determining its presence and amount, it none the less is a distinct aid in diagnosis. Palpation of the stomach has in his opinion not received the attention it deserves, but other means of examining the stomach like gastroscopy, gastrodiaphany he passes over briefly as having proved themselves of little worth. To those interested in gastric diseases this book will be serviceable.

Makers of Man. A Study of Human Initiative. By Charles J. Whitby, M. D. (Cantab.) $3.00. (*New York: Rebman Company, 1911.*)

From the preface we learn that the author has "essayed the experiment of dealing with the lives of great men as problems capable, through and through, of psychological treatment and elucidation. Even their physical organisms are, from this point of view, to be regarded not as mere animated 'matter,' but each one as organized experience, a psychosis, the sub-conscious and super-conscious factors of which all play their part in contributing to the feeling tone, modifying the opinions, or determining the motives of conduct." The subjects chosen are forty world-famous individuals.

The book consists of thirteen chapters, four of which are continuations, and these are headed: Introductory, Classification, Family History, Parentage and Constitution, Physical Characteristics, Natural Vocation, The Natural History of Purpose, Power in the Crucible, Limitation and Crime, and Individuality: Its Nature and Power.

The above may be considered as viewpoints from which the author considers the lives of Julius Cæsar, Charlemagne, William the Silent, Sir Francis Drake, Cardinal Richelieu, Oliver Cromwell, Frederick the Great, Lord Nelson, Napoleon Bonaparte, Abraham Lincoln, Dante, Leonardo da Vinci, Titian, Cervantes, Mozart, Goethe, Beethoven, Sir Walter Scott, Turner, Gustave Flaubert, Bacon, Galileo, Harvey, Descartes, Spinoza, Sir Isaac Newton, Leibnitz, Kant, Hegel, Charles Darwin, Jesus Christ, St. Paul, Marcus Aurelius, St. Augustine, St. Gregory the Great, Mahomet, St. Francis d'Assisi, Martin Luther, Ralph Waldo Emerson, and Ernest Renan. Surely, excellent material.

The author has given us an intensely interesting book besides one of great value to the physician, psychologist, sociologist, eugenist, etc. The work has been excellently and most successfully done, and should be in the library of everyone interested in the uplift of the race or individual. Even one who is merely in search of entertaining reading will be well repaid by its perusal.

W. R. D.

Report of the International Plague Conference. Held at Mukden, April, 1911. (*Manila Bureau of Printing, 1912.*)

The feature of this report which stamps it with exceptional interest is the fact that the Conference was called by the Chinese Government and that Chinese physicians took an active part in the discussions. This demonstrates in a striking way the advance of the medical practitioner in China, and as time goes on there is not the least doubt but that important contributions to medicine will come from that country. Perhaps the most remarkable characteristic of the plague epidemic which existed in Manchuria and northern China in 1910-11 was its pneumonic form—the bubonic form practically not occuring at this time. The disease was doubtless contracted by hunters from a species of marten, known as the tarbagan, and spread from the hunters to the coolie class, which was the one that suffered most. The report which covers the bacteriology, pathology, clinical data, epidemiology, measures employed to combat the disease, etc., has been admirably prepared by Dr. Richard P. Strong, and will serve as the basis for all future reports on epidemic pneumonic plague. Thus the Conference will have proven of lasting benefit to the world.

Infantile Paralysis in Massachusetts During 1910. Together with Reports of Spinal Investigations Made in 1911 Bearing upon the Etiology of the Disease and the Method of its Transmission. (*Boston: Wright & Potter Printing Co., State Printers, 1912.*)

This report is reprinted from the Monthly Bulletins of the Massachusetts State Board of Health, and makes a most important addition to the literature of Infantile Paralysis. It is a great satisfaction to have the papers, some of which have appeared previously in various medical journals, thus reprinted with an abundance of illustrative maps. All interested in the epidemiology, as well as other features of the disease, will find this report most instructive.

The Prevention of Dental Caries. By J. Sim Wallace, M. D., L. D. S., etc. Second Edition. 1/6. (*London: Office of The Dental Record, 1912.*)

The author's studies have led him to the belief that caries is due, in large measure at least, to the "highly refined carbohydrate foods," while "foods of a more fibrillar or fibrous character," which he calls "detergent," are less likely to induce this trouble. The latter help to cleanse the teeth during the chewing process, while the former stick to the teeth and are not easily removed. It is questionable whether this is the fundamental cause of caries, but, in any case, it seems likely to play a part, and if this small volume teaches its readers nothing more than the necessity of the constant use of a tooth brush it will serve a good end.

A Handbook of Practical Treatment. Edited by John H. Musser, M. D., LL. D. and A. O. J. Kelly, A. M., M. D. Volume III. (*Philadelphia: W. B. Saunders Company, 1912.*)

The review of this book had just been completed when the news of the death of Dr. Musser was received. It is a sad coincidence that both of the editors of this work should have died so soon after its completion. There were few men more beloved by the profession than Dr. Musser. He was above all the clinician so far as concerned his professional work, but apart from this, his interest in the younger men of the profession was always strong. The untimely death of Dr. Kelly was a great loss to American medicine, but he has left his mark on the medical literature of his generation.

The third and final volume of this work keeps up the standard set by the previous ones. Constitutional diseases, those of the respiratory, digestive, urinary and nervous systems, and mental diseases are discussed. In a work such as this it is not possible to review every part in detail. The section dealing with constitutional diseases gives a very complete discussion of the treatment of these difficult problems. Dr. Futcher has written several of the sections in his usual clear and thorough manner. His reference to chronic rheumatism is to be highly commended. In the discussion of the diseases of the respiratory system several subjects were taken by the senior editor, whose discussion of them is full and satisfactory. In the section on gastric neuroses more attention might have been given to the importance of treatment of the general condition; reference is made to it, but this is one of the important points which would be the better of greater emphasis. We are too much given to paying attention to the relief of symptoms and losing sight of the essential causal condition and perhaps to no group of disorders does this apply with more force than to

the gastric neuroses. The trouble is usually more with the patient than with his stomach. Dr. Stockton contributes an excellent section on diseases of the liver which covers the subject very fully. A very important question—that of visceroptosis—is discussed by Dr. Sailer. This is well worthy of commendation and discusses a difficult subject very fully and well. Dr. Spiller takes the organic diseases of the nervous system and Dr. Taylor, the spinal meninges and cord. These articles are comparatively short but seem quite adequate. Dr. Dercum deals with the functional nervous disorders in a very satisfactory way.

Throughout the work the discussion of the surgical treatment is taken up fully and the editors have been fortunate in the men chosen for this. These sections are satisfactorily done throughout. It is becoming more and more the custom to take up the "borderland" subjects from both the medical and surgical sides, and very properly so. In the past there has been too little coöperation.

The work as a whole is a great addition to our literature on therapy and can be confidently recommended as a guide in treatment.

The Medical Annual. A Year Book of Treatment and Practitioner's Index. Thirtieth year. 9/6. (*Bristol: John Wright & Sons, Ltd., 1912.*)

This Annual is prepared with care by a large number of practitioners in various countries (England, France, Austria, India, the United States). Surgery and Medicine are both well covered, as one can judge from the fact that there is a chapter on Ionic Medication, one of the very latest developments in medicine. It is supplied with an excellent index, and numerous useful illustrations. There is much information in the volume of use only to the British practitioner, but anyone anxious to learn the progress that has been made in any special branch of medicine during the past year will find this volume most serviceable. The Annual is an excellent reference handbook.

The International Medical Annual. A Year Book of Treatment and Practitioner's Index. Thirtieth Year. $3.50. (*New York: E. B. Treat & Company, 1912.*)

This is merely the American edition of the Year Book of Treatment noted above, with the parts alone of service to English practitioners omitted.

Lateral Curvature of the Spine and Round Shoulders. By Robert W. Lovett, M. D. Second Edition. Revised and Enlarged. Illustrated. $1.75. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

Those who know the first edition of this work will want the second. It is a work designed essentially for the orthopedist, and no one in America has given more attention to this special branch of medicine than Lovett. From the careful anatomical and clinical studies made by him, his conclusions should be attentively studied by those working in the same field. If more physicians and surgeons would write similar monographs, instead of attempting to cover the whole field of medicine and surgery, many more valuable treatises would be published than appear now. Here is a subject well handled by one who has studied it most thoroughly and made himself master of its difficulties.

Surgical Operations. A Hand-Book for Students and Practitioners. By Prof. Friedrich Pels-Leusden, Berlin. Only Authorized English Translation by Faxton E. Gardner, M. D., New York. Illustrated. (*New York: Rebman Company, 1912.*)

The Rebman Company is doing a valuable piece of work in furnishing translations, to American doctors, of important foreign medical books, and "Surgical Operations" is one of the best of its series. As chief surgeon to one of the largest surgical clinics in Berlin, Pels-Leusden writes from a large and varied experience, and it is of distinct advantage for men who cannot travel or read foreign languages to have this opportunity to study the views of one of the leading operators of Europe. There is no lack of excellent surgeries both for the student and practitioner, but many will be glad to add this book to their libraries. After introductory chapters on Antisepsis and Asepsis, Anæsthesia, and Division and Reunion of the Different Tissues, the author takes up the Surgery of the Blood-vessels, Operations on the Extremities, Operations on the Head, Neck, Chest, Surgery of the Abdomen, and Urinary and Genital Organs. It is a typical German production in the vague lack of reference to the work of foreigners, but this in a way makes the book more valuable as representing modern German surgery, and to change but slightly a phrase in the author's preface, "those who will seek advice in this book will find its reading fruitful." It is a well-illustrated work of about 700 pages with good type and paper.

Infections of the Hand. A Guide to the Surgical Treatment of Acute and Chronic Suppurative Processes in the Fingers, Hand, and Forearm. By Allen B. Kanavel, M. D. Illustrated with 133 Engravings. $3.75. (*Philadelphia and New York: Lea & Febiger, 1912.*)

The book is divided into two parts. The first deals with simple localized infections and allied minor clinical entities. The second takes up grave infections, as follows: (a) Discussion of diagnosis and treatment in general; (b) Tenosynovitis and fascial space abscesses; (c) Acute lymphangitis and allied infections; (d) Complications and sequelæ of acute infections.

The work is based on careful experimental and anatomical investigations in conjunction with accurate clinical observations on a large number of cases.

Infections of the hand and forearm are very common and nearly every medical man feels competent to take care of such cases. However, many of these infections are treated without regard to definite anatomical knowledge of the part, and while a number of them recover with a functional result which is sometimes good, on the other hand we all see results which are distinctly bad, and which are due, in many instances, to a lack of knowledge of the structures and spaces involved.

The book is well gotten up and the illustrations are excellent. The descriptions are for the most part clear.

It is, indeed, a pleasure to read such a thorough exposition of a subject, and Dr. Kanavel is to be congratulated on this valuable piece of work. The volume should be in the library of every surgeon and will also be of great use to the general practitioner.

J. S. D.

Surgery of Deformities of the Face, Including Cleft-Palate. By John B. Roberts, A. M., M. D., etc. Illustrated. $3.00. (*New York: William Wood & Co., 1912.*)

This work founded on the Mütter Lectures of the College of Physicians of Philadelphia, delivered by the author in 1900 will be of assistance to all surgeons. Plastic operations are among the most difficult that a surgeon meets with, and this accounts in some measure for the lack of development in this branch of surgery—though it seems also as if it required a man with very special gifts of patience, foresight, and delicacy of hand, to obtain good results in such work. One necessarily hesitates to attack a severe deformity of the face lest the patient may not only be no better but possibly worse off after the operation. Careful study of Roberts' book will help many a surgeon in a tight place, and it is so well and abundantly illustrated that the operator who for the first time tackles one of these delicate cases will find here all the assistance he can obtain in any book—for his success he must have those same gifts which the author has, as shown in his results.

An Index of Differential Diagnosis of Main Symptoms. By Various Writers. Edited by Herbert French, M. D. Oxon., etc. Illustrated. 30/. (*Bristol: John Wright & Sons, Ltd., 1912.*)

A few sentences from the preface will best indicate the scope of this comprehensive work. "The book is a treatise on the application of differential diagnosis to all the main signs and symptoms of disease . . . . It covers the whole ground of medicine, surgery, gynecology, ophthalmology, dermatology, and necrology. . . . Its articles on various symptoms are arranged in alphabetical order. Whilst . . . . the general index at the end gathers these together under the headings of the various *diseases* in which they occur." As the editor points out both text and index should be used together, as otherwise the reader may miss a number of places in which diagnosis is discussed, for each symptom is classified but once under its own head, while a disease may be referred to many times under different symptoms. Many prominent English physicians have contributed to this volume, as Bosanquet, Buzzard, Cammidge, Garrod, Hertz to mention only a few well-known names, but these are sufficient to indicate that the work has been done with thoroughness by leaders in their specialties. There is no doubt that a book as carefully prepared as this has been will prove very serviceable, especially to students and young practitioners; and in obscure cases, to the older practitioner also. The different sections are signed by their respective authors, which adds, we feel, weight to the articles. This Index is a valuable addition to the armamentarium of the physician, and both the editor and his collaborators deserve hearty praise for the successful accomplishment of this exhaustive undertaking. The publishers are also to be complimented on their part of the work—the type is necessarily small, but it is clear, and the illustrations are satisfactory.

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London Practitioners' Manuals. Anæsthesia and Analgesia. By J. D. Mortimer, M. B. (Lond.), F. R. C. S. (Eng.). 1911. 16°. 276 pages. University of London Press, London.

London Practitioners' Manuals. Minor Surgery. By Leonard A. Bidwell, F. R. C. S. With eighty-eight illustrations. 1911. 16°. 265 pages. University of London Press, London.

American Gynecological Society. Transactions. Volume 36, for the year 1911. 8vo. 605 pages. Philadelphia.

Studies from the Rockefeller Institute for Medical Research. Reprints. Volume XIII. 1911. 8vo. New York.

Index-Catalogue of the Library of the Surgeon-General's Office, United States Army. Authors and Subjects. Second series. Vol. XVI. Skinko-Stysanus. 1911. 4to. 882 pages. Washington.

Serum Diagnosis of Syphilis and the Butyric Acid Test for Syphilis. By Hideyo Noguchi, M. D., M. Sc. 14 Illustrations. Second edition. 1911. 8vo. 238 pages. J. B. Lippincott Company, Philadelphia and London.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by Leighton F. Appleman, M. D. Volume IV. December, 1911. 8vo. 326 pages. Lea & Febiger, Philadelphia and New York.

The Bellevue Hospital Nomenclature of Diseases and Conditions. With Rules for the Recording and Filing of Histories. Compiled by the Committee on Clinical Records, composed of Robert J. Carlisle, M. D., Warren Coleman, M. D., Thomas A. Smith, M. D., Edmund L. Dow, M. D. Adopted by the Board of Trustees, 1903. Revised and made to conform to the International Classification. 1911. 16°. 328 pages. New York.

Nachweis und Bestimmung von Giften auf biologischem Wege. Eine Anleitung für Pharmakologen, Gerichtsärzte, Gerichtschemiker und Apotheker. Von Dr. phil. et med. Hermann Fühner. Mit 89 zum Teil farbigen Textabbildungen. 1911. 8vo. 176 pages. Urban & Schwarzenberg, Berlin und Wien; Rebman Company, New York.

Urology. The Diseases of the Urinary Tract in Men and Women. By Ramon Guiteras, M. D. (Harv.). With nine hundred and forty-three illustrations in text and seven plates. 1912. 8vo. Two Volumes. D. Appleton & Co., New York and London.

A Treatise on Tumors. By Arthur E. Hertzler, M. D., Ph. D. Illustrated with 538 engravings and 8 plates. 1912. 4to. 725 pages. Lea & Febiger, Philadelphia and New York.

Die experimentelle Pharmakologie als Grundlage der Arzneibehandlung. Von Dr. Hans H. Meyer und Dr. R. Gottlieb. Zweite, neubearbeitete Auflage. Mit 64 zum Teil farbigen Textabbildungen und 1 farbigen Tafel. 1911. 8vo. 554 pages. Urban & Schwarzenberg, Berlin und Wien; Rebman Company, New York.

Second Review of Some of the Recent Advances in Tropical Medicine, Hygiene and Tropical Veterinary Science. Being a Supplement to the Fourth Report of the Wellcome Tropical Research Laboratories at the Gordon Memorial College, Khartoum. By Andrew Balfour, M. D., B. Sc., F. R. C. P., Edin., D. P. H. Camb. and Captain R. G. Archibald, M. B., R. A. M. C. in collaboration with Captain W. B. Fry, M. R. C. S., L. R. C. P. and Captain W. R. O'Farrell, L. R. C. P. & S. I., R. A. M. C. 1911. 4to. 448 pages. Published for Department of Education, Sudan Government, Khartoum, by Baillière, Tindall & Cox, London; Toga Publishing Company, New York City.

The Surgery of Oral Diseases and Malformations. Their Diagnosis and Treatment. By George Van Ingen Brown, D. D. S., M. D., C. M. Illustrated with 359 engravings and 21 plates. 1912. 8vo. 740 pages. Lea & Febiger, Philadelphia and New York.

Honan's Handbook to Medical Europe. A Ready Reference Book to the Universities, Hospitals, Clinics, Laboratories and General Medical Work of the Principal Cities of Europe. By James Henry Honan, M. D. With maps of Berlin, Edinburgh, London and Paris. 1912. 12mo. 261 pages. P. Blackiston's Son & Co., Philadelphia.

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INTESTINAL OBSTRUCTION: A STUDY OF THE TOXIC FACTORS.

By Harvey B. Stone, M. D., Bertram M. Bernheim, M. D., and George H. Whipple, M. D.

(From the Hunterian Laboratory, Johns Hopkins Medical School, Baltimore.)

No introduction to this work is more natural than a narrative of the manner in which we became interested in it. In the spring of 1911, two of us were doing some operations for the late Dr. A. H. Koelker,[1] who desired some pure pancreatic juice and duodenal secretion for the study of synthetic peptids. In order to obtain the duodenal secretion free from other digestive juices, we isolated the lower portion of the duodenum, from a point just distal to the lower pancreatic duct to the beginning of the jejunum, and reëstablished the alimentary canal by anastomosis of the stump of the duodenum to the upper jejunum. Believing that a delayed opening of the isolated loop would involve less risk of soiling the wound and the abdominal cavity, this loop was pulled up into the incision, which was closed about it, and the drainage of the closed loop postponed with the intention of doing it a day or two later. To our disappointment, however, all of these dogs, three in number, died within the first twenty-four hours, before drainage was established. At the first occurrence of this phenomenon we were inclined to attribute the outcome to some surgical error. When careful autopsies on all the cases failed to reveal any apparent cause for the result, other than the lack of drainage of the closed loop, we decided to try the same operation with the addition of an immediate enterostomy into the isolated portion of the duodenum. We succeeded in this way in providing Dr. Koelker with a dog from which he obtained the desired duodenal secretion. This dog was used by Dr. Koelker for several months in Baltimore, and was taken by him to New York and is perhaps still living. In considering the facts just related we were struck at once with the relation they bore to the problem of the cause of death in intestinal obstruction, and we felt that they suggested a method by which some of the problems connected with this great question might be solved. It is the result of this work, still incomplete but sufficiently advanced to justify this report, with which we are now to deal.

Intestinal obstruction from its great clinical importance and interesting physiological aspects, has of course been the subject of much experimental work and there has developed about it an extensive literature. At this time we shall attempt no exhaustive review of the latter, contenting ourselves with a summary of the more recent work. Three classical explanations have been given of the cause of death in obstruction; first, infection; second, nervous reflexes; third, intoxication.

[1] Koelker, A. H.: Ztschr. f. physiol. Chem., 1911, LXXVI, 27.

The third explanation is capable of subdivision into two groups of ideas as to the source of the toxic material. One of these attributes the noxious substance or substances to the activities of bacteria within the alimentary canal. The other theory postulates a secretion of the poisons by the glandular structures of the digestive tract. To these views must now be added a fourth, championed especially by Murphy and Vincent,[2] who in a recent publication say, "Interference with the circulation of the obstructed intestine is a vital factor in the production of the symptoms of ileus," and venous obstruction is the most important element in this circulatory interference. Before reporting the details of our own work, and discussing its bearing on these theories, the important facts already established that relate to the general problem will be reviewed briefly.

In a paper appearing quite recently, and directed along much the same lines as our present work, Hartwell and Hoguet[3] have shown by bacteriologic examinations on dogs with high intestinal obstructions that death may result without demonstrable invasion by organisms of the blood stream, peritoneum, liver or spleen. This and other work practically rule out the infection theory. There is no direct evidence to support the nervous reflex hypothesis and there is good experimental evidence against it. As to the origin of the supposed toxins—bacterial or secretory—certain observations generally accepted furnish collateral evidence of some importance. Thus J. W. Draper,[4] formerly known as J. W. D. Maury,[5] showed conclusively, in a long series of experiments, that obstructions high in the intestinal tract are much more quickly fatal than those situated lower down. This is in accordance with general clinical and experimental experience. It is also a well established fact that the bacterial flora of the alimentary tract is relatively poor about the duodenum and upper jejunum, and grows much more luxuriantly as one precedes aborally. These two facts taken in conjunction have led Roger[6] and others to feel that the bacterial explanation of the source of toxic substances is fallacious, since the part of the intestine poorest in bacterial inhabitants is that which yields the most rapidly fatal result when obstructed. As opposed to the position of Roger, Murphy and Vincent believe that the toxic substances are purely bacterial in origin, basing their opinion on observations they made as to the behavior of these substances. We feel that the conclusions reached by these authors are drawn from insufficient premises, and certain of our results do not agree with the observations reported by them. Further the importance attached by Murphy and Vincent to circulatory disturbance is not borne out by certain of our experiments, nor by closely similar experiments performed by Hartwell and Hoguet. These writers were able to produce typical obstructive symptoms without the element of circulatory interference, and the same findings were observed in the experiments now to be detailed.

[2] Murphy and Vincent: Boston M. & S. J., 1911, CXLV, 684.
[3] Hartwell and Hoguet: Am. J. M. Sc., 1912, CXLIII, 357.
[4] Draper, J. W.: J. Am. M. Ass., 1911, LVII, 1338.
[5] Maury, J. W. D.: Idem, 1909, CXXXVII, 725.
[6] Roger: Presse méd., 1911, I, 1.

Our first experiment has already been referred to. Four dogs were operated upon as follows—ether as in all these experiments being the anæsthetic. The duodenum just below the distal pancreatic duct was divided, the ends being closed and inverted. The gut was again divided in a similar manner at the beginning of the jejunum. An isolated loop from twelve to fifteen centimeters long was thus formed. The gastro-intestinal canal was then reëstablished, either by an end to end or lateral duodeno-jejunostomy, or by a posterior gastro-enterostomy and the abdomen closed.

As an example of this group the following protocol will serve.

Operation October 23, 1911, 3 p. m. Isolated loop of duodenum 15 centimeters long. Posterior gastro-enterostomy. Closure.

October 24, 11 a. m. Dog is dull. Tremors and staggering in hind legs. 2 p. m. much more drowsy, marked muscular tremors all over. Staggers badly when trying to walk. Pulse weak and rapid. 4 p. m. died with increasing general weakness and tremors.

All these dogs died within 28 hours. The post-operative course was fairly characteristic. With the exception of one or two attacks of vomiting in two of the dogs, they seemed as well as ordinary post-operative animals until within from two to five hours of the end. Then the animal would become noticeably dull and apathetic. Slight muscular tremors began. The gait became difficult and sidling. The hind legs especially seemed ataxic and the animal frequently staggered sidewise with his hind quarters. Weakness and muscular tremors rapidly increased, the pulse became remarkably weak and thready. Vomiting was usually absent. There was no noticeable abdominal distention. There seemed to be no pain. This picture is described in some detail because it is the same that was met with in the various experiments subsequently performed, and will not be again rehearsed.

As was said in the first instance, we were struck by the fact that we had here a fatal experimental condition, certainly closely resembling ileus, yet much simpler, for if one assumed that the obstruction of the loops was the cause of death, any part that might conceivably be played by the bile, pancreatic secretion, and gastric juice, in clinical death from obstruction, was reasonably well eliminated here. The same could also be said of products derived from ingested food stuffs. To remove any question as to the possible significance of the small amount of these substances that remained enclosed within the loop at the time of operation, five dogs were prepared in which at operation the loop was washed through with two or more litres of water, until the washings came away entirely clear.

To illustrate this group we quote the following experiment.

Operation November 9, 1911, 6 p. m. The usual loop of duodenum was isolated by division and washed through with two litres of sterile water. The ends of the divided intestine were all closed. The loop thus occluded was dropped back into the abdomen and a posterior gastro-enterostomy done. Closure.

November 10, 3 p. m. Dog listless, slightly ataxic, tremors, 4.30 p. m. Much weaker. Marked staggering. 8 p. m. found dead.

Of this series one dog died in twenty-seven hours and one in forty-eight. The other three were killed in twenty-four, twenty-eight and forty hours, respectively. This was done in order to secure ante mortem blood for study. It would appear from this series that washing the loop somewhat prolonged life, but the series is too small and the difference too slight to attract attention. Nor do we maintain that every dog so prepared would die within the limit of forty-eight hours, the limit attained by our longest post-operative life. Sufficient cases are here recorded to prove, however, that these high loop occlusions are rapidly fatal.

In view of the importance attributed by certain writers, notably Murphy and Vincent, to the part played by vascular disturbances and to simplify still further the experiment, another modification was made in the operation. Instead of the division and inversion of the ends of the loop, which necessarily involves a certain amount of interference with circulation, in five dogs the gut was not cut. Occlusion was secured by tight double ligatures at either end of the loop, passed between the mesenteric attachment of the gut and the arcade of vessels in the mesentery. The vessels were quite undisturbed and the only vascular interference was in the narrow circle of gut immediately within the grip of the ligatures. This constricted area was covered by approximating the serous surfaces of the gut above and below the ligature with mattress sutures, thus burying the ligatures. The washing was done by introducing tubes through small incisions in the bowel wall, which were afterward carefully closed. In order to avoid injured areas within the loop under observation, these wounds were made, respectively, above the point selected for the oral ligature and below that for the aboral ligature, the irrigation being

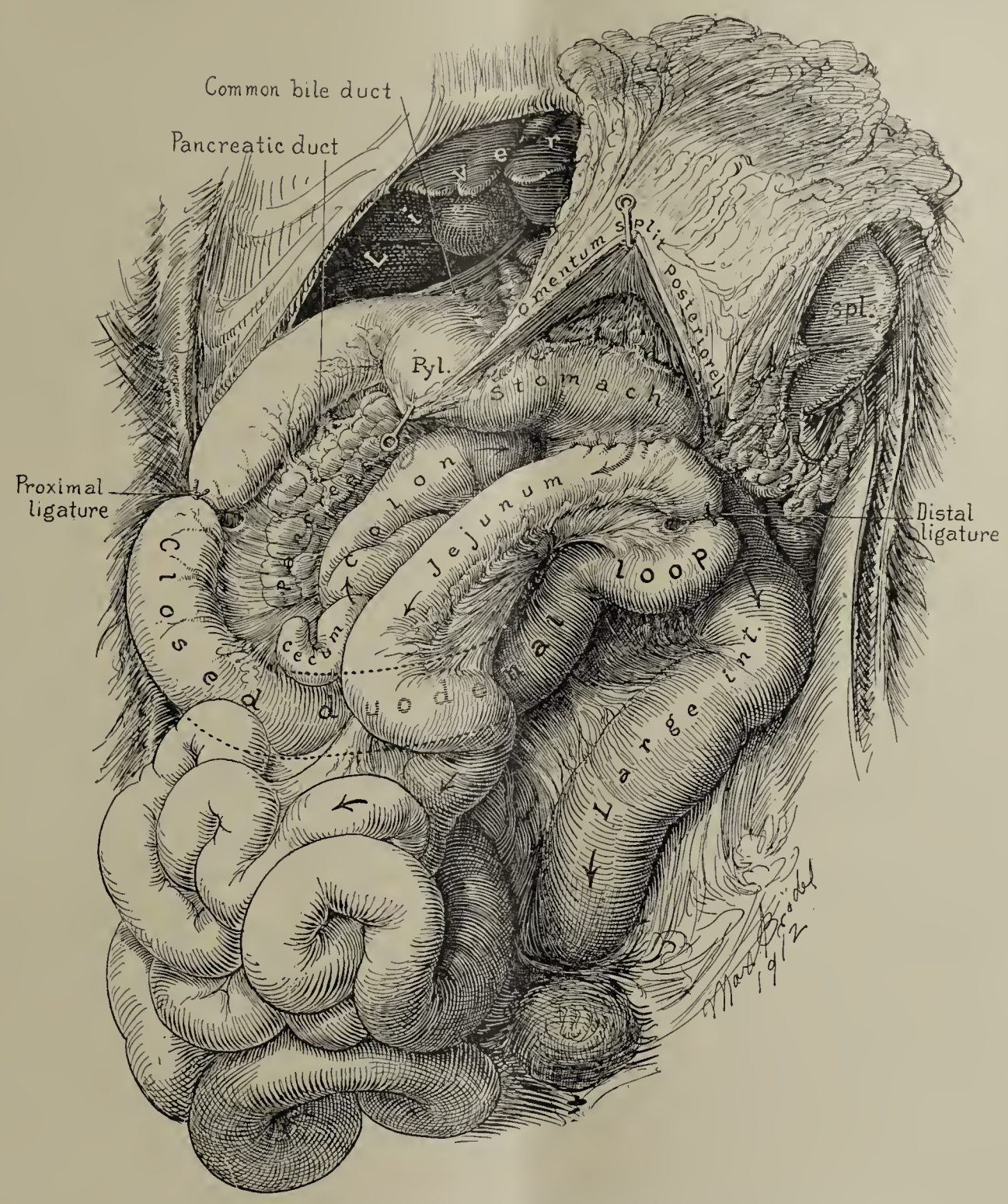

Fig. 1.—The usual type of operation in making a closed duodenal loop showing the portion of duodenum involved.

limited to the gut between the two incisions for the tubes by placing temporary intestinal clamps just outside the limits of these two incisions (Fig. 2).

Of this series the following case will serve as an example. Operation January 19, 1912, 2 p. m. Loop washed and ligated above and below as just described. Posterior gastro-enterostomy. Closure.

January 20, 3 p. m. Dog showing toxic symptoms. Killed to secure material for study.

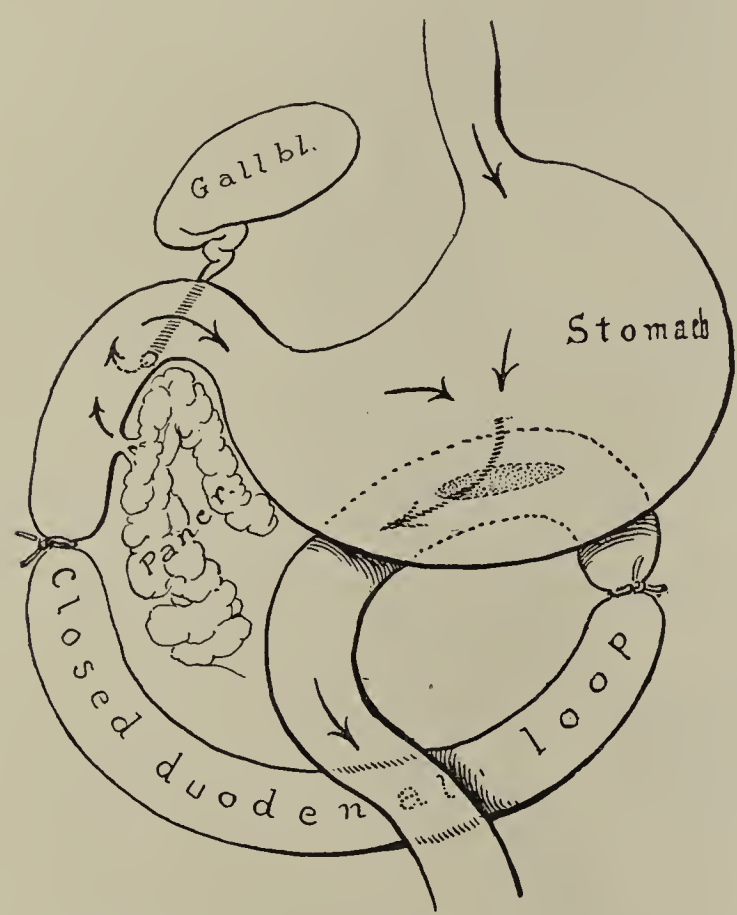

Fig. 2.—Diagram to show the path of secretions around the isolated duodenal loop.

Autopsy Findings.

Dogs which die as the result of a closed duodenal loop present a pretty uniform picture. It makes very little difference whether the death results in 24 hours or 72 hours. We may describe the general picture as follows: The thorax, heart and lungs are negative. The spleen, pancreas, kidneys, adrenals and blood vessels are normal. The peritoneal surface usually shows a slight amount of peritonitis over the closed loop, gluing it to the adjacent loops of bowel. This is a dry plastic peritonitis with grains of fibrin and some injection of the serous surfaces, but no exudate. The peritoneum is dry rather than moist. The liver may show some congestion and in some cases a little fatty degeneration. The *closed loop* is practically the only structure that deviates from the normal. It is invariably enlarged and distended with fluid, its walls often mottled with purple areas of hemorrhage and stippled with grains of fibrin. In some cases there may be greenish or charred looking areas in the wall where there is obvious necrosis and we have observed one case where there was a rupture through such an area with escape of the fluid into the peritoneum and death in 27 hours.

The fluid in the loop is very characteristic, a dirty slate or dull red colored fluid, about the consistency of thick soup, often containing considerable mucus, blood and desquamated mucosa. The odor is unpleasant and suggests hydrogen sulphide. The mucosa of the loop may be intact and show only a diffuse reddening and swelling but more often is specked with ecchymoses or shows shallow ulcers with red swollen margins. The inverted ends of the loop may show some digestion and hemorrhage.

The stomach usually contains a considerable excess of bile stained fluid, but the mucosa is normal. The intestine is usually quite clear and presents a pale normal mucosa.

Microscopical sections show normal organs except possibly in the case of the liver where there may be some fat present in very tiny droplets and an excess of polymorphonuclear leucocytes in the capillaries. The duodenal loop shows an acute inflammation, especially in the region of ulcers when they are present. There may be necrosis, hemorrhage, oedema and a marked infiltration by wandering cells, particularly the polymorphonuclear type. Other parts of the loop may show merely a trifling oedema and superficial inflammation involving only the tips of the villi.

The individual variation of dogs to the poisonous action of this closed loop is considerable, but it is unusual for a dog to live longer than 48 hours. If a dog is killed with ether at the end of 24 hours when he does not seem much intoxicated, the findings at autopsy are very different from those described above in the fatal cases. In this instance, the viscera are quite normal. The peritoneum shows a few grains of fibrin and a loss of gloss, due to the slight peritoneal injury necessitated by the operative trauma. The duodenal closed loop in this instance is collapsed and quite flabby. On opening through the wall one sees an intact mucosa which is of a dull pinkish color and slightly swollen. There are no ulcers or hemorrhages. The loop contains no fluid but only one or two cubic centimeters of thick tenacious brown or blood-stained mucus. Yet this material when washed out carefully with water can be shown to contain large amounts of the toxic substance present in the duodenal fluid so abundant in the fatal cases.

Microscopical study shows normal organs. The duodenal loop is lined by a mucosa which is practically normal. There is a trifling injection of some of the capillaries in the villi and a few leucocytes sometimes in such areas.

A possible explanation of the result noted is that we had thrown out of function an organ essential to life. An analogy to an excretory organ like the kidney, or an organ of internal secretion perhaps, might be assumed. To secure evidence in this direction we excised the loop in question, since if either of the above suppositions were correct, it would presumably be quite as fatal to excise as to occlude the loop. A number of attempts were made which resulted unsuccessfully, the dogs dying after a number of days of various incidental conditions including distemper, pneumonia, and intussusception. One dog, however, lived in good condition for eight weeks after this particular loop had been excised. One such positive result

is sufficient to show that this part of the duodenum is not essential to life.

As has been said, we found that drainage of the occluded loop saves the animal's life. We have successfully repeated this experiment, and dogs have lived with closed duodenal loop and fistula for six or eight weeks. It is not an easy operation to perform, however. A number of attempts failed and all for the same reason. After living a variable period, from two to five days, the drainage became insufficient either from inflammatory swelling of the ends of the loop with closure of the lumen, or from a sphincter-like action of the recti muscles, or from occlusion by blood clots. These dogs died with the symptoms before noted and were found to have loops distended with the same material encountered in the closed loops. In the dogs which survived, the symptoms of intoxication had begun to develop when prompt irrigation of the loop, repeated on several occasions until spontaneous drainage became free, abated the evidence of obstruction and undoubtedly saved the animals' lives.

From these facts, the obvious inference is that the loop contains some highly poisonous material. The conclusive proof of this fact is shown by the injection of this material into normal dogs, the effects of which will soon be described. We have undertaken a few experiments to compare the high loop which has been the exclusive subject of consideration hitherto, with other parts of the small intestine. It is well known, as has been noted above, that high obstructions are more rapidly fatal than low. It has been shown by several investigators, possibly first by Halsted,[7] that dogs with isolated loops from the low ileum may live for several weeks or months. We therefore attempted no control series of low loop dogs from the point of comparative post-operative longevity, using them simply as a source of material for comparison with that obtained from the high loop dogs. It is worthy of note, however, that even a low loop dog which, owing to some technical error, developed peritonitis, lived six days, far beyond any period reached in our series of high loop dogs.

We believe that we may fairly conclude from these data that the cause of death is to be sought in the absorption of some toxic material within the closed loops, and that the high loops contain more of this material or a more active form of it, than the low loops. There seem to be but two possible sources for this toxic material—secretions from the mucous membrane of the loop, and the products of bacterial life within the loop. At present we feel strongly that the secretory theory is the more probable, and, although unable conclusively to exclude bacteria from any part in the toxin production, we believe that such part, if it exists at all, is subsidiary in importance. This in spite of the work of McClure,[8] who showed the enormous multiplication of organisms that takes place in the contents of obstructed loops. The facts upon which these opinions rest are the mechanical removal of most of the bacteria by washing the loops; examination of the loop contents culturally at death, which shows abundant but not enormous numbers of organisms; the rapidity of death in the high loop dogs, which seems almost too quick to be caused by elaboration of bacterial toxins; and the fact which has made so much impression on other observers, that in the low loops where organisms are so preponderatingly more numerous death may not supervene for weeks or months. A decisive experiment would be the complete destruction of either the mucosa or the bacteria. So far we have not been able to secure such a crucial test. Efforts to destroy the mucosa by means of chemical agents have failed in this but have quickly killed the animal itself. However, we hope that further researches in this direction may be more successful in the near future.

The death of animals in which obstruction was uncomplicated by any circulatory interference, a result corroborated by the work of Hartwell and Hoguet just published, makes it difficult to accept the importance of this factor in death from ileus, so emphasized by Murphy and Vincent. Of course it is quite true that when one adds to obstruction of the intestinal lumen an infraction of the gut produced by profound circulatory interference, as was done by Murphy and Vincent, there is every reason to expect more fulminant and disastrous reactions than in simple obstruction alone. But to assume therefore that the circulatory interference is the vital factor in the production of the typical symptoms of ileus is not only an unwarranted deduction as a matter of logic, but is contravened as a matter of fact by the observations of Hartwell and Hoguet and by our own. It is obvious that the demonstration of the rapidly fatal results from isolation of washed high loops, and of the highly toxic nature of their contents, consisting only of secretion and some bacteria is not without scientific interest. It at least suggests the value of further study of abnormal intestinal secretion from this point of view, nor is the matter devoid of some practical interest as well. We realize that our experimental conditions do not duplicate exactly the condition of clinical ileus, but the relation is certainly close. In an obstructed bowel encountered at the operating table, containing food substances, bile, gastric and pancreatic juice, as well as the intestinal secretion proper, there may be and quite probably are numerous other toxic bodies besides those whose presence we have demonstrated. But the latter alone are sufficient to cause rapid death, and our loop experiments have shown the importance of thorough and early drainage, especially in high obstruction. Washing the stomach and regurgitant fecal vomiting may be compared to the incomplete drainage that was unable to save a number of our dogs. The suggestion also arises that in those cases of obstruction where the surgeon is in doubt whether to close the abdomen or establish intestinal drainage (and perhaps no problem requires nicer surgical judgment), a border line case when situated low in the gut might be safely closed, and should be drained if placed in the upper loops. This in spite of the well known risks of skin digestion and starvation with high enterostomies. The danger of rapid toxic death is a more pressing consideration than either of these objections. Lastly there is the not unreasonable hope that a further study of the toxins, whose origin and properties are somewhat narrowed down by this work, may put into our pos-

[7] Halsted, W. S.: Am. J. M. Sc., 1887, XCIV, 436.

[8] McClure: J. Am. M. Ass., 1907, XLIX, 1003.

session some means of combating their effects, pending surgical relief of the mechanical conditions that make them dangerous. Already we have some suggestive evidence that a dog injected with a sub-lethal dose of the toxic material is not so rapidly killed by obstruction.

Toxic Substances Present in the Closed Duodenal Loop and Their Action upon Normal Animals.

The "duodenal fluid" which accumulates in these closed duodenal loops may be presumed to contain the toxic substance or substances responsible for the death of these animals suffering from intestinal obstruction or occluded intestinal loops. We expect to give a detailed account of these findings in the near future, but will outline here the facts which have come out of this work up to the present time.

This duodenal fluid is usually faintly alkaline to litmus, but contains no hydrogen sulphide as its odor suggests. It coagulates into a firm mass at the boiling point and a considerable precipitate comes down on heating at 60° C. for 10-20 minutes. This fluid may be heated at 60° C. for hours, centrifuged at high speed and filtered in any way desired without lessening in any way its toxic powers. This procedure gives a dirty brown or slate colored, opalescent fluid with characteristic odor. This fluid is very toxic to normal animals and 10-20 cc. introduced intravenously will usually kill a healthy dog of 10-15 lbs. weight.

The reaction of a healthy dog to this fluid introduced intravenously is so characteristic and constant that we need only describe one experiment. Following the injection, as a rule, there is a rapid fall of blood pressure followed by a prompt return to normal, but this is not invariable and is of no importance. This prompt depressor action can be produced by any type of extract made from the intestinal mucosa. The important vascular reaction is a slow steady fall in blood pressure which may not be evident before 30-60 minutes but progresses to a very low level and is associated with a slight slowing of the pulse. This fall is accompanied by a great dilatation of the vessels in the splanchnic area and probably in great part dependent upon it. At this time the blood is incoagulable or clots very slowly and will inhibit normal blood coagulation. Antithrombin is present often in great amounts. There is increased secretion of fluid in all the intestines with appearance of fluid stools from the rectum. The temperature of the animal falls rapidly in spite of the presence of abundant artificial heat, reaching even 30° C. (rectal) shortly before death. The blood pressure in dogs fatally poisoned never returns to normal, but rather sinks slowly even to ¼ or ⅕ that of normal. The respiration becomes very slow and gasping with prolonged and forceful inspiration. The pupils are widely dilated.

Death supervenes usually in 2 to 6 hours, and if the dog lives 12 hours one may expect a rapid recovery to normal during the following day.

The autopsy findings in such a dog fatally poisoned by the duodenal loop fluid are very constant. The blood shows considerable concentration, yielding perhaps only ¼ to ⅓ its volume of plasma after centrifuging. The dried weight may go as high as 26% or 27%. The heart contains but little blood, as most of it is to be found in the splanchnic area. The blood usually clots very slowly or not at all, due to the presence of an excess of antithrombin. The serous cavities, heart, lungs and kidneys show nothing of interest. The spleen, liver and pancreas show engorgement and the liver may feel very tense and friable. The splanchic veins in the mesentery and serosa of the intestines are very conspicuous. The stomach shows a pale mucosa usually but may show some reddening of its cardiac portion. The pyloric portion is always pale. The *duodenum* beginning one centimeter below the pylorus shows a *deep red* or *purple* velvety mucosa which contrasts vividly with the pale mucosa just above it. This purple mucosa may be coated with more or less mucus and associated with a good deal of thin watery fluid. This condition usually is less intense in the jejunum and fades to a pink or pale red in the ileum. The large gut may be free from this change or present a deep red mucosa.

Histological study shows nothing of importance in the viscera. The purple color of the mucosa of the small intestine is seen to be due to a great engorgement of all the capillaries in the villi. There is no inflammatory exudate here. There may be some escape of blood into the stroma of the villi or into the interglandular tissue of the mucosa (large intestine) but this is usually absent or inconspicuous.

This *toxic substance* or compound seems to act particularly upon the splanchnic vessels and this is probably its dangerous feature. We have been interested to determine, if possible, what the nature of this substance might be, but have only a few points to offer as yet. It is removed from the duodenal loop fluid by heat at 100° C. which causes a massive coagulation. It is not destroyed by autolysis at 38° C. with chloroform and toluol even after a period of 6 to 8 weeks.

It is not destroyed by pancreatic digestion for at least seven days. It is not destroyed by putrefaction for a few days, but we cannot say positively about prolonged action of bacteria.

It is probably destroyed by hydrolysis with 5% sulphuric acid for 6 hours at 100° C. but this point too is uncertain at present. This substance does not stimulate the pancreas to activity as does "secretin," for instance. The toxic material is equally powerful whether introduced into the jugular or into the portal vein.

We have been unable to obtain this substance in any manner except by obstruction of an intestinal loop. The blood in animals which are moribund from the effects of a closed duodenal loop, is not in any way toxic to a normal dog. Autolysis of normal intestinal mucosa at 38° C. with chloroform and toluol for days or weeks furnishes no toxic material. Autolytic material from one entire normal intestine will not injure a small dog, whereas the autolysed mucosa from a closed duodenal loop 15-20 cm. in length will yield a fatally poisonous substance. Putrefaction of the intestinal mucosa gives a very unpleasant fluid but this heated at 60° C. and filtered is not toxic, even in large amounts, up to 50-70 cc. Hydrolysis with 5% sulphuric acid at 100° C. using normal intestinal mucosa

or tissue from various organs will not yield any similar toxic substance.

It may be objected that this substance is not the one concerned in the intoxication of the animals with closed duodenal loops but careful analysis offers many points of similarity.

The animals injected with the duodenal loop fluid show a slowly falling blood pressure and temperature, which symptoms are present too in the dogs with closed duodenal loops. The injected animals excrete large amounts of fluid into the intestine, causing diarrhoea and escape of fluid from the rectum even under anaesthesia. This pouring out of fluid into the intestines is a striking feature in any high intestinal obstruction and conspicuous even in these duodenal loop dogs.

The mucosa of the closed duodenal loop shows abnormal reddening and injection—not comparable, however, it is fair to say, to the mucosa of the injected dogs. The manner of death in profound shock with very slow deep gasping respiration is very similar in the dogs with closed duodenal loops and the animals injected with the duodenal loop fluid. We have some evidence too that repeated injections of duodenal loop fluid in sublethal doses makes an animal more resistant to large doses of this duodenal fluid and most important of all *resistant* to poisoning by a closed duodenal loop made in this animal at some later time. This too speaks in favor of this toxic factor being one and the same in the injection experiments and in the closed duodenal loop experiments. Because of the individual variation of dogs to this poison much evidence must be accumulated to establish this point.

It will occur to one at once that the picture of *anaphylaxis* in dogs presents many features in common with the poisoning due to injected duodenal loop fluid. Recently a healthy dog (weight 21 lbs) sensitized to human serum was injected with a large amount of human serum (140 cc.) after an interval of one month. The blood pressure promptly fell and remained low until death in two hours. The blood clotted very slowly. The temperature fell rapidly. The viscera at autopsy were negative except for congestion. There was an escape of semi-fluid stools during the last hour of life. The *intestinal tract* presented many interesting points. The stomach was normal. The duodenum was somewhat injected and mottled purplish red. The jejunum and ileum showed a velvety red mucosa, the color becoming more intense in the ileum, very similar to that described in the dogs poisoned with the duodenal loop fluid. The distribution here was different, being more intense in the ileum instead of the duodenum. The mesenteric vessels were all very conspicuous. The striking similarity of this picture (anaphylaxis) with that of poisoning by duodenal loop fluid suggests a possible relationship between this substance elaborated in the closed intestinal loops and the substance which is set free in the dog's body following the second injection of a foreign proteid.

Summary.

High loop obstruction in dogs causes very rapid death, 24 to 60 hours as a rule, even when the loop contains no food material nor secretion from the stomach, liver and pancreas. Low loops (ileum) of similar nature are much less rapidly fatal.

Surgical drainage of this loop will save the dog's life.

Excision of this duodenal loop does not necessarily disturb the animal's health.

The material obtained from obstructed loops is toxic when injected into dogs, the high loop material being much more toxic. This material causes profound splanchnic paralysis with extreme congestion of all this area—particularly the small intestine.

The toxic material introduced into normal animals produces many changes similar to those found in the animals with closed duodenal loops—namely, low blood pressure and temperature, excretion of large amounts of fluid into the intestinal canal and fatal shock.

This toxic substance given in a single injection causes a reaction in the dog which is almost identical with the picture of anaphylaxis in this animal.

The toxic material is not injured by heating at 60° C. for any length of time, centrifuging and filtering in any manner. It is not impaired by prolonged autolysis, by pancreatic digestion and bacterial fermentation. Hydrolysis with dilute acids probably destroys it.

No such toxic substance may be obtained by autolysis, digestion or putrefaction of the normal intestinal mucosa.

Injections of sublethal doses of this toxic material will protect against subsequent large doses and probably prolong life after a closed duodenal loop has been established.

PRIMARY CARCINOMA OF THE LIVER.*

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The fundamental problems of the pathology of primary carcinoma of the liver are still unsettled. They relate to the histogenesis of the tumor, its relation to cirrhosis of the liver, the origin of the multiple tumor nodules, their growth and the absence of extensive extrahepatic metastases. After a brief review of the views concerning these subjects the results of the study of six cases of primary cancer of the liver will be reported.

General Considerations.—Primary cancer of the liver is very rare occurring only in .28% (v. Hansemann [1]) to 3% (Goldzieher and v. Bokay [2]) of all autopsies in the various statistics.

* A more detailed article including complete case reports will be published in the next volume of the Johns Hopkins Hospital Reports.

The latter percentage is high, and the incidence of the tumor as given by most authors is less than 1%. It is most frequent in adult males, but is relatively common in adult females. It may occur at any age, and a few cases have been described in infants. Clinically the condition is difficult to differentiate from cirrhosis of the liver. Its rapid course, the presence of an enlarged irregularly nodular liver, hemorrhagic ascites or metastases in accessible regions, which is exceedingly rare, may be of assistance in the diagnosis.

Histogenesis.—The presence of bile pigment is of relative value in the differentiation of cancers arising from the liver cells from those arising from the bile duct epithelium. While bile stained tumors are, as a rule, derived from the liver cells, tumors arising from the epithelium of the smaller bile ducts may contain bile pigment within their lumina (Fischer,[3] Herxheimer,[4] Loehlein[5]). Microscopically these two groups may be differentiated by the following characteristics: They teud to conform to the structure of the tissue from which they arise, the bile duct cancers are, as a rule, tubulo-adenomatous, the liver cell cancers trabecular in structure (Hanot and Gilbert,[6] Eggel,[7] etc.). Their cells tend to conform to the cell of origin, those of the bile duct cancers are cubical or cylindrical with clear protoplasm and chromatin rich nuclei, those of the liver cells are larger, polygonal or polyhedral with a granular protoplasm and more vesicular nuclei (Goldzieher and v. Bokay,[l.c.] etc.). The stroma is of greatest importance. The bile duct cancer always has a connective tissue stroma which divides it into alveoli, while the liver cell cancer only has a capillary stroma and is composed of this stroma and the columns of tumor cells alone (Weglein,[8] Dibbelt,[9] Yamagiwa[10]). Through anaplasia the liver cell cancer in areas may form rosettes, where several rows of cells are arranged with their long axis perpendicular to the axis of a central canal, or they may assume a tubular structure (Goldzieher and v. Bokay,[l.c.] Yamagiwa,[l.c.] etc.).

Relation to Cirrhosis.—Liver cell cancers occur with cirrhosis in from 75% to 100% of the cases reported by Eggel,[l.c.] Yamagiwa[l.c.] and Goldzieher and v. Bokay,[l.c.] while bile duct cancers are associated with cirrhosis less frequently, 42% to 62% in the same statistics. In most instances the cirrhosis is annular, but other forms and those consequent upon syphilis, chronic passive congestion (Yamagiwa) and parasites such as schistosomen eggs (Yamagiwa) and echinococcus cysts have been described (Bamberg, Dibbelt,[l.c.] Loehlein[l.c.]). It seems, therefore, that cancer of the liver may be associated with any disease of the organ where there is a regeneration following an injury.

Every possible hypothesis regarding the relation of the cirrhosis to the tumor formation has been advanced: (1) The two processes were considered entirely independent by Kelsch and Kiener,[11] Frohman,[12] etc. The latter came to this conclusion because the most cirrhotic areas in his preparations were free of tumor nodules. (2) The opinion that both conditions resulted from a common cause has been adandoned, since in some cases the cirrhosis was of syphilitic or parasitic origin. (3) The third possibility that the cirrhosis was secondary to the tumor formation had several phases. Marckwald[13] suggested that the irritation of the tumor development led to cirrhosis even in those portions of the liver uninvolved by the growth. This did not seem plausible since similar tumors occurred without cirrhosis. On the other hand with extension of the cancer into the capillaries, atrophy and necrosis of the liver cells may result followed by condensation and new formation of connective tissue (Ziegler[14]). (4) Finally in most instances the cirrhosis precedes the cancer and is the direct cause of the neoplasm. This theory was first advanced by Sabourin.[15] Schmieden[16] went further and regarded the hyperplastic liver cell islands so common in cirrhosis as the precancerous stage. This has been upheld by most of the subsequent writers (Eggel,[l.c.] Theodorow,[17] Weglein,[l.c.] Loehlein,[l.c.] Milne,[18] Goldzieher and v. Bokay,[l.c.] Yamagiwa,[l.c.] etc.). These authors do not offer Ribbert's theory concerning tumor formation but believe that consequent to injury there is destruction of liver tissue which is followed by regeneration. As a result of a repetition of this cycle, following Weigert's conception, certain cells through proliferation exceeding their goal become cancerous.

This hypothesis has been utilized further to explain the greater frequency of liver cell to bile duct cancers with cirrhosis. After experimental injury the connective tissue liver cells and bile ducts all take part in the repair. The liver cells are the most active (Podwyssoski) and it may be concluded that they have a greater proliferative capacity and therefore are more often stimulated to cancer formation.

Mode of Growth.—The transition pictures described at the periphery of the smaller tumor nodules are in large part responsible for the confusion which still exists concerning the mode of growth of the cancer. It was believed that the columns of liver cells were in many instances directly continuous with the columns of tumor cells and that the capillaries of the liver and tumor were directly continuous in these areas (Schuppel,[19] v. Heukelom,[20] Travis,[21] etc.). This led to the conclusion that the tumor increased in size by a progressive metamorphosis of liver cells to tumor cells as had been described by Waldeyer in skin cancer and Hauser in gastric cancer. On the other hand, Heussi[22] believed that the above transitions were artifacts brought about by the tumor cells growing between the capillaries and destroying the liver cells. He consequently denied appositional growth and was sustained in this by Ribbert,[23] Herxheimer,[l.c.] Fischer,[l.c.] Eggel,[l.c.] etc. The latter pointed out that similar transition pictures occurred in metastatic growths where the secondary nature of the tumor was unquestionable (Ribbert, Perls, Naunyn, Schmidt). Weglein[l.c.] described similar transitions in the center of nodules of primary cancers of the liver and considered them to be artifacts possibly dependent upon a difference in the appearance of tumor cells at different ages, etc. The transition pictures have received decreasing attention in recent years. They either have not been observed at all or are found rarely (Eggel,[l.c.] Goldzieher and v. Bokay,[l.c.] Yamagiwa[l.c.]). Those authors who emphasize the above transitional pictures advocate the multicentric origin of the tumor (v. Henkelom,[l.c.] Travis,[l.c.]

Loehlein[l.c.] (one case), Goldzieher and v. Bokay,[l.c.] Yamagiwa,[l.c.] etc.). Yamagiwa contends that cancer of the liver is multicentric in origin since both forms frequently arise on the basis of a regeneratory hyperplasia of liver cells or an inflammatory hyperplasia of bile ducts, both of which occur in many areas: i. e., multicentric.

Heussi[l.c.] and his teacher, Ribbert,[l.c.] stand alone as advocates of the unicentric origin of cancer of the liver though their theory has been accepted in individual instances by Weglein, Loehlein, Fabian,[24] etc. They emphasize the well known fact that the tumor invades the portal vein by predilection. It may then fill the portal and even the hepatic vein with cancer thrombi and in such cases these thrombi cut in cross section will give the appearance of multiple tumors. Ribbert says in several instances it was possible to pull the tumor out of the branched bed of the portal vein in cast-like form and in this way by far the greater part of the tumor could be removed from the liver. In other instances, where the occlusion of the vein is not so evident, the multiple tumors result from embolic transplantation of tumor cells broken off from the primary tumor which has invaded the vascular stream.

Relation to Adenomata.—On account of the frequent occurrence of cancer of the liver with cirrhosis, it is believed that most of these tumors pass through the benign stage of nodular hyperplasia or adenoma. The cases unassociated with cirrhosis are considered by Ribbert,[l.c.] Yamagiwa,[l.c.] etc., to arise from misplaced embryonic rests. They are confirmed in this view since cancer of the liver without cirrhosis is most frequent in childhood.

Extrahepatic metastases occurred in 66 of the 163 cases collected by Eggel.[l.c.] They occur earlier and are more frequent in cancers arising from the smaller bile ducts than from those of the liver cells. Those from the liver cell cancers are never extensive and form inconspicuous nodules in the thoracic and mesenteric lymph glands, lungs, etc. The almost constant invasion of the venous system makes the infrequency of metastasis more obscure. Weglein believes that they may be encapsulated or destroyed in the pulmonary vessels.

During the past year several cases of primary liver cell cancers were observed. These offered confirmatory evidence of certain of the above views and as a result the six cases occurring in the pathological services of the Johns Hopkins Hospital and Bay View Hospital were examined. The results will be briefly summarized.

General Consideration.—Three cases occurred in the first 3700 postmortem examinations at the Johns Hopkins Hospital, a percentage of 0.8. In four cases where this was ascertainable the disease occurred in adult males between the 4th and 6th decades. Clinically they corresponded to the usual types.

Histogenesis.—In all of the above cases the tumor originated from the liver cells themselves. The cells of the tumor resembled the liver cells. They were somewhat smaller, had a less regularly granular protoplasm which had a much greater affinity for hæmatoxylin than the protoplasm of the liver cells. With hæmatoxylin and eosin the protoplasm of the tumor cells stained pale blue while that of the liver cells stained pink. The nuclei were, as a rule, larger and more vessicular than those of the liver cells, but the size of the nuclei and their chromatin content varied considerably and small pyknotic ones were not infrequent. Mitotic figures were always demonstrable in the tumor nodules, and cells with several nuclei were found here and there.

The tumors had a trabecular structure and were composed of columns of cells similar to those of the normal liver acini, though, as a rule, these columns were much thicker and often had ten or more cells abreast. In some instances these were so thick that solid nests of cells were formed. Between the columns or surrounding the solid nests was a layer of endothelial cells. These were part of the capillary stroma, which occurred throughout the tumor. No definite connective tissue stroma was to be found in any of the cases. In some instances the tumor had a more glandular structure. All transitions occurred from simple crevice-like dilatations between the cells of the columns to lumina, similar to those of the bile ducts and rosette-like nodules. The latter were composed of a variable number of rows of tumor cells arranged with their long axis perpendicular to a central lumen as in a perithelioma. The various cavities in the tumor nodules cut longitudinally were short and the cells surrounding many of them were compressed. Their possible production by simple dilatation of pre-existing intercellular spaces or bile capillaries as suggested by Yamagiwa, etc., seems plausible. The more definite structures, like the rosettes which occurred particularly in the tumor thrombi, are probably the result of a reversion of the tumor to the embryonic structure of the liver. These glandular and tubular structures were not sufficiently conspicuous in any case to confuse the picture.

Necrosis occurred particularly in the larger tumor thrombi and in many smaller tumor nodules. In many of these there were multiple centers of necrosis and in this way false glandular structures were produced. Cells in process of disintegration often resembled the normal liver cells closely. Their protoplasm stained pale pink and their nuclei were smaller and more deeply staining.

Relation to Cirrhosis.—In all of the cases there was a marked cirrhosis besides the multiple tumor nodules. In two, however, relatively large areas of liver, uninvolved by tumor nodules, were entirely free of the cirrhotic process. On further examination, the following facts, which, of course, are well known, but which are not usually emphasized, became evident: The liver suffers greatly from the presence of the tumor. The tumor nodules compress the surrounding liver tissue which may be seen as concentric layers of more or less atrophied columns of liver cells. In many places the liver cells have entirely disappeared, and in their place there is a condensation and a fibrosis of the preexisting stroma. This appears as dense bands of fibrous tissue more or less completely surrounding the larger tumor nodules. In other areas the plugging of the vascular trunks results in a tremendous dilatation of the intraacinar capillaries. This is associated with

an atrophy of the liver cells and in some areas these processes are so extensive that a picture similar to an angioma is produced. In still other areas definite necrosis of the hepatic parenchyma occurs probably brought about by the extensive tumor thrombi.

In these three ways, at least, fibrosis may result from the effect of the cancer upon the hepatic parenchyma and bring about a cirrhosis secondary to the tumor growth. An analogous process was described by Ziegler l.c. in his text-book, but Eggel was unable to find any similar cases in his exhaustive review of the literature in 1901, and since his time the possibility of a picture simulating a true cirrhosis, but secondary to the tumor growth, has not been emphasized. In some instances, also, so much of the liver is involved by the tumor that it is difficult to obtain areas, of any sufficient size uninvolved by tumor, to study the cirrhotic process, and in these it may be impossible to determine the relation between the two conditions.

In four cases the cirrhosis was marked even in those areas uninvolved by tumor. It is, therefore, evident that the cirrhosis is not entirely dependent upon the new growth in all cases and the general consensus of opinion, that the cirrhosis precedes the neoplasm, is probably correct. Whether a picture of cirrhosis may be produced secondary to the tumor growth cannot be said with certainty from the other two cases. It is evident that the cirrhotic process is exaggerated greatly, both macroscopically and microscopically, as a result of the innumerable tumor nodules scattered through the hepatic parenchyma.

Mode of Growth.—In order to understand the nature of the transition pictures between liver and tumor cells at the periphery of the tumor nodules, and the apparent multicentric origin of the neoplasm, the grosser details of the tumor growth will be considered first.

In all of the six cases many of the blood vessels contained tumor thrombi. In several, where the entire liver could be studied, these tumor thrombi were by far the most conspicuous part of the growth. They formed long strands and streamers which could be followed through and dissected from the portal vessels. Nodular enlargements were also found along their course and these even occurred at the very periphery just under the capsule of the liver. Naturally the conclusion was reached that the tumor started in one area invaded the portal system, and in this way involved more or less of the liver secondarily. This was the more interesting since a preceding report of one of these cases from this laboratory had considered that the tumor was multicentric in origin, and that transitions between liver cells and tumor cells were demonstrable at the periphery of the nodules.

These cases were, therefore, carefully investigated. In two the extensive macroscopic tumor thrombi were confirmed and emphasized by the microscopic picture. The great majority of the tumor nodules were contained within the portal veins. The vessel wall in most instances still had an intact endothelial lining, the elastica could be readily stained and where these were not sufficient serial sections showed the connection between the tumor nodules and the thrombus. Such a thrombus cut longitudinally showed a most characteristic picture. Its branches corresponded with the vascular bed, and these varying sized ramifications invaded the liver tissue everywhere as larger and smaller strands, sheathed by a varying sized vessel wall in a more or less perfect state of preservation. In one case the large portal vein at the hilus of the liver was invaded by the large tumor in the right lobe of the liver, but as was seen in the gross examination, the thrombus did not invade all of the branches of the vein supplying the left lobe. Microscopically also many of the portal branches were free of tumor cords, but on the other hand, many of the tumor nodules were surrounded by endothelium. Throughout, pictures similar to those described were found, and this was true also of the other three cases.

Pictures suggestive of transitions between liver cells and tumor cells at the periphery of the smaller nodules occurred, but these were rare and they did not form a distinct group. Various relations between the tumor nodules and the hepatic parenchyma were found. Some nodules, as we have seen, were definitely enclosed within a thick walled vein, others invaded the vein wall or grew out through a thinner walled vessel into the hepatic parenchyma. In many of these only remnants of the thinned vessel wall remained in one area. Around these nodules the columns of liver cells were frequently flattened and compressed as above described, while in others, cords of tumor cells ran out into the intraacinar capillaries or through the vein wall into the liver columns themselves. In these latter instances pictures resembling transitions between liver cell and tumor cell occurred. These, however, were rare and in view of the numerous intermediary stages and the vascular invasion, it seemed hardly necessary to assume that these were actually transitions.

The presence, therefore, of a larger nodule in the right lobe of the liver and the extensive plugging of the portal radicals with tumor thrombi led to the conclusion that the tumor was unicentric in origin in all these cases and that the multiple nodules were in part sections of tumor cords which filled the portal vein, in part the result of emboli from the same source. Fabian had reached the same conclusion in regard to his case, as may be gathered from the following sentence: "The invasion of the lymphatics and blood vessels seems to be an important characteristic of this type of tumor, and though no actual invasion was noted under the microscope in this case, it has been seen in other instances. Given an invasion of the portal system with new growth, the diffuse distribution throughout the liver is easily accounted for."

While it is impossible to draw any sweeping conclusion concerning the unicentric origin of primary cancer of the liver from so few cases, there are certain well known facts which strengthen this conception. The very definition of the cancer arising from the liver cells is dependent upon the fact that it invades the blood vessels and only in this way does it differ, in many instances, from the benign adenoma. This was emphasized by all of the older writers and v. Heukelom, l.c. particularly, pointed it out, mentioning its occurrence in more

than three-fourths of the cases reported. In his own cases he could not exclude the possibility that the tumor had invaded the liver through the portal vein but this he considered improbable on account of the pictures of transition. In Eggel's l.c. series, also, venous tumor thrombi were a most frequent occurrence, and it is not unlikely that it occurs in every case where multiple tumor nodules are found in the liver.

With tumor thrombi occurring constantly it would seem that nothing further were necessary to explain the multiple nodules and that they were simply metastases. v. Heukelom could not accept this view on account of the frequent transitions between liver cells and the tumor cells at the periphery of the small nodules. These transitions now, however, have become far less important, and as we have seen are on the one hand not accepted by many and considered as rare occurrences by the remainder. It seems, therefore, that it may be said with reasonable assurance that primary cancer of the liver is unicentric in origin, as a rule, at least, and that in most instances, if not always, the so-called transitions are artifacts. Yamagiwa's l.c. argument that the cancer is multicentric in origin because hyperplastic liver nodules occur in many areas, i. e., are multicentric, may be theoretically correct, but there seems no basis for the assumption that if one hyperplastic nodule acquires cancerous manifestations that this should occur in many such nodules.

The theory that these tumors increase in size by a constant metaplasia of liver cells to tumor cells has been less and less advocated as the so-called transitions became rarer and better understood. In the above cases there was no evidence to support this theory of appositional growth, but the presence of numerous mitoses as is usually found in malignant tumors seemed to indicate that the growth of the neoplasm was entirely autogenous.

Extrahepatic Metastases.—Even though metastases occurred in the lungs in the four cases of the above series where complete protocols could be had, the metastatic nodules were very small. This is not what might have been expected with the extensive vascular involvement that was present. In several instances the tumor grew up the cava and into the pulmonary artery, still there were only a few nodules in the lung tissue.

The absence of extensive extrahepatic metastases in cancer of the liver has been repeatedly emphasized. This is, of course, not unique for this tumor, but the question why certain tumors metastasize generally, while others, like the cancer of the prostate, have a predilection for bone, etc., is of the broadest interest. It is not only true of neoplasms, but occurs likewise with various infectious processes.*

Summary and Conclusions.

Primary carcinoma of the liver is a rare condition, occurring in 0.28% to 3% of all autopsies from various statistics.

It occurs most frequently in adult males, but is proportionately relatively common in females and may occur at any age. A number of cases have been described in infancy.

Clinically, the disease is difficult to differentiate from cirrhosis of the liver. Its rapid course, the presence of an enlarged, irregularly nodular liver, hemorrhagic ascites, or metastases to accessible regions, which is exceedingly rare, may be of assistance in the diagnosis.

The tumor may occur in normal or in diseased livers. In a tremendous percentage of cases the liver presents an ordinary type of cirrhosis, but various other types of chronic hepatitis caused by syphilis, parasites, etc., may occur. The tumor itself may be only one large nodule. This may have smaller ones at its periphery and in this way transitions occur until the entire organ is studded with varying sized nodules. Any division between these forms is simply arbitrary and subserves no useful purpose.

The tumor may arise either from the smaller bile ducts or from the liver cells. The names carcinoma cholangiocellulare and carcinoma hepatocellulare may be used to differentiate them as suggested by Goldzieher and v. Bokay.l.c. The liver cell tumor may be bile stained, but this does not differentiate it absolutely from the duct cancer, for bile pigment may be found in the lumina of the latter nodules. The liver cell cancer has a trabecular structure; it is composed of thick columns of cells not very unlike normal liver cells which may be arranged in solid nests and show here and there a glandular structure. Its stroma is always composed of a simple capillary net similar to the interstitial tissue of the liver acinus. The bile duct cancers have a tubulo-adenomatous structure and have a more or less dense connective tissue stroma.

It is generally agreed that the cirrhosis precedes the neoplastic formation where these two are associated. The tumor, however, brings about pressure atrophy directly and necrosis of the hepatic parenchyma through its extensive vascular involvement, and in this way a fibrosis may result secondary to the tumor growth. This is important since in a few cases those areas of liver uninvolved by tumor growth are likewise free of cirrhosis. Whether a cirrhosis may be produced secondary to the tumor is uncertain, but there is no doubt that the cirrhotic process is exaggerated greatly as a result of the tumor growth.

The secondary formation of cancer as a result of a chronic destructive process in the liver parenchyma finds its analogue in many malignant tumors elsewhere in the body. It may be interpreted in the following way: as a result of the destruction there is a constant demand for repair. The cells proliferate and loose their more specific functions until finally the equilibrium between function and growth is lost and certain cells become vegetative. The constant occurrence of the reparative phenomena is manifested in the liver by the hyperplastic liver nodules so frequently found in cirrhosis and these are supposed by many to be the source of the liver cell cancers.

Primary cancers of the liver are differentiated from benign adenomata chiefly by their power to invade the blood vessels. The portal vein is most frequently invaded and all of its radicals may be plugged with tumor thrombi. In some instances practically no tumors remain after the growth in the blood vessels is removed. But in any case where there is an invasion of the portal system the diffuse distribution in the liver

* This has been discussed by me in an article upon Primary Tuberculosis of the Spleen to appear in the June, 1912, number of the Archives of Internal Medicine.

is easily accounted for. The so-called transitions from liver cells to tumor cells at the periphery of the tumor nodules are denied by many, and considered to be extremely rare by most of the rest of the writers since v. Heukelon. In most instances they are probably artifacts brought about by an invasion of the liver acini by the tumor thrombi or emboli. Granted this, there is no longer any basis either for the multicentric origin of cancer of the liver or that its subsequent development is brought about by an appositional growth.

The tumor is not in any respect unique. It is unicentric in origin, distributes itself through the vascular system, forming a more or less diffuse growth in the liver and develops autogenously. The rarity of extensive extrahepatic metastases in view of the tremendous tumor thrombi which not only involve the portal, but also the hepatic veins and the vena cava is worthy of note.

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A METHOD OF CORRELATED TEACHING OF PATHOLOGY AND BACTERIOLOGY IN THE SECOND YEAR OF MEDICAL INSTRUCTION.

By Frederick P. Gay,

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The continually increasing scope of each of the medical sciences has of necessity led to a differentiation in the interests of those seriously enrolled in any one of them. For effectiveness it has become essential for the individual to restrict his research in large measure to the single field in which he is most interested. Teaching, too, to be most stimulating and critical would preferably cover only such ground as the instructor can know at first hand. An ideal curriculum, then, in any one of these sciences would consist of a well-balanced, co-operative course covering the entire field and subdivided in such a way that each division may be in charge of an instructor whose first interests are therein represented. It may be that such was the plan in many of the older medical centers, although it is certain that fewer highly trained and whole time men have been available in the past to carry out such a purpose. Even if such were the original scheme of instruction, the essential combination of the scheme was frequently broken, in providing for the independence of an associate in the way of a separate department. It is far from my purpose to advocate any system that militates against the rise and independence of the individual, but the fact seems clear that the essential inter-relation of such a curriculum as will be described would be impracticable in separate departments. It may not be supererogatory to express the belief that individual growth is best fostered by transplantation.

It is the privilege of workers in newer communities to try rather comprehensive schemes of development that would be quite impossible in more traditional surroundings. The method of teaching the second year course in pathology in the University of California is a case in point, and, from its apparent success with small classes of students would seem worthy of description.

In view of the restricted and incorrect use of the term it is not gratuitous to define the science of pathology as concerned with the *entire* natural history of disease. The expression "science of Pathology" is premeditated as expressing an

academic, biological entity, brought to the attention of the medical student in his second year before immersion in clinical interests that of necessity demand a more utilitarian or applied type of pathology. It would seem best, then, to teach students first the broadest possible conceptions of disease processes, considered each as a whole through the successive stages of causation, progress, and effect. Equally effective results are not obtained by the usual method of studying the typhoid bacillus in one term followed months later in another course by a study of the lesions it produces. This artificial separation of bacteriology from morbid anatomy and histopathology, moreover, has apparently not served to accentuate but rather to conceal the usual deplorable hiatus that should be filled by a functional pathology.

The novelty of our method of instruction lies, not so much in an appreciation of its advantages, as in the opportunity for carrying it out. The concentration system has been put in force for the first two years' instruction in our medical school. As a result, the student enters the second semester of his second year (January to May) with physiology, physiological chemistry, pharmacology, and anatomy (with the exception of two half days a week in regional anatomy which includes auscultation and percussion) off his hands. His work in the department of pathology and bacteriology comprises, therefore, four whole days a week (32 hours) for seventeen weeks (544 hours). The average class at present numbers about twenty men and women and the teaching staff consists of three full time ranking men, and one half time assistant. In a general way, the work is divided into three closely correlated parts in each of which one of the full time teachers is particularly experienced and interested and for which he is responsible. The four forenoons of the week are devoted to histopathology, morbid anatomy (including individual experience in autopsy work), the experimental production of lesions in animals, and general histopathological technic. The afternoons are divided nearly equally between general bacteriology and experimental work in infection and immunity. The class exercises both in histopathology and in bacteriology are usually preceded by an introductory talk; more formal lectures in these subjects are regarded as unnecessary in view of the existence of wholly adequate text-books to which students may be referred. A more formal set of lectures, two a week, covers the intermediate field between the better recognized branches of pathology, by discussing the progress of each disease that is being synchronously studied in respect to cause and effect. The elaborateness and practicability of the data of infection and immunity renders their study particularly fitted to represent this field of functional pathology. The rapid development in these subjects, moreover, admirably exemplifies the value of the experimental method in the study of disease.

The barest outline of such a combined method of teaching pathology would appeal at once, but the logical fascination of the scheme and some evidence of its actual didactic value appear more fully in considering details of the work as carried out.

The course begins with an introductory lecture in which an attempt is made to show the intimate relationship between the three parts of the course and their relative importance. It is pointed out that bacteriology and morbid anatomy are subjects of which the methods and the major facts are known; for this reason they are easier to teach and offer less fruitful fields for research. The field of functional pathology is at once less well known and more difficult to teach; it is, however, not only from motives of intellectual curiosity but also from its practical value in aiding diagnosis and treatment of disease, of pre-eminent importance. Owing to the limitations of time and indeed of the instructor, but one phase of functional pathology is emphasized. The data collected under the head of immunology, however, present at once the most accessible and at the same time most practical phase of the subject. It is frankly pointed out that either pathological physiology or pathological chemistry might almost equally well serve to bridge the usual chasm between cause and effect. An attempt is made further to explain the differences between acute infectious, metabolic, chronic diseases, and diseases of unknown origin. With this outline of pathology schematically depicted the actual work is begun.

The forenoons of the first week are occupied by a histological study of human lesions grouped to cover the general aspects of degeneration and pigmentation. This would seem the best method of transition from normal histology to histopathology. Gross specimens whenever available are demonstrated and the class begins work in groups by producing similar lesions in animals, experimental jaundice in the dog by ligation, cloudy swelling and hemoglobinuria due to cantharadin poisoning in the rabbit, phosphorus poisoning, necrosis due to ligation of vessels, and the like.[1] Two men are assigned to each experiment the significance and method of which is explained to them. They are then purposely left largely to themselves with the expectation that they may not succeed in obtaining the results expected on first trial; the experience of failure being regarded as of more value than immediate success. They are, however, responsible, for a report on their work and are expected to demonstrate their results to the rest of the class. The corresponding afternoons of the first week are occupied in learning the standard methods of preparing culture media.

The bacteriological work of the second week includes culture methods for saprophytic bacteria: preparing plate cultures, staining methods including demonstration of spores and the appearance of involution forms in old cultures; and the bacterial production of nitrites, indol, and fermentation in sugar media. The lecture course begins at this point with two lectures on the general problems of infection. The work in morbid anatomy includes the classical types of inflammation in prepared sections, the study of the frog's mesentery, and inflammation of the rabbit's ear by hot water and croton oil. The students who actually prepare these animals for the class demon-

[1] These experiments and many in following days are based on the exercises outlined by Pearce in his admirable article on "The Teaching of Experimental Pathology and Pathological Physiology, etc." Johns Hopkins Hospital Bulletin, 1911, XXII, 404. I am greatly indebted to Professor Pearce for placing advance sheets of his experiments at our disposal before publication.

stration are further taught how to fix, section, and stain the tissues for comparison with the more complete series of slides that have already been given them for microscopic study. The entire class is thus eventually instructed practically in the usual histological methods either from similar experimental material or from post mortem tissues. This work continues in the third week with studies of other forms of inflammation and abcess formation produced by the pyogenic cocci. These pyogens are at the same time being studied in the afternoons both culturally and in connection with exercises on phagocytosis both of the simple and induced type (opsonic). These latter experiments are carried out by the entire class. The lectures of this period cover natural immunity, Metchnikoff's theory of phagocytosis, and phagocytosis as increased by the opsonins of normal serum. Two students inject rabbits, one intravenously, one subcutaneously, with virulent cultures of *M. aureus,* demonstrate the pyemic abcesses when they occur, and carry through the tissues both for technical reasons and for comparison with the lesions on hand. The whole class carries out the Neisser-Wechsberg bioscopic test for leucocidin with materials obtained by injecting rabbits with cultures of *M. aureus.*

During the fourth week abcesses and repair are studied not only anatomically and histologically but experimentally through the preparation of clean and infected wounds in animals. Bacteriologically smears of the meningococcus from the spinal fluid, and of the pneumococcus in pneumonic sputum, are studied. Individuals inject the sputum in a rabbit and a mouse and isolate a pure culture. Cultures of the gonococcus are shown, smears of gonorrhœal pus studied, and cultures of the *M. melitensis* are given out for growth on the various media. The pathogenesis and specific therapy of the coccal infections are considered in lectures.

Histologically the fifth and sixth weeks are occupied in the study of circulatory diseases, embolism, thrombi, infarcts, and the like, supplemented by the experimental production of bland infarcts and thrombi (Pearce: Exercises IV, 1, 3, and 4). Diseases of the heart are likewise covered. The afternoon work of the fifth week is largely concerned with a study of the streptococcus, its production of hemotoxins, group experiments demonstrating positive and negative chemotaxis of leucocytes by virulent and non-virulent strains (Bordet) and experiments to show the protective value of antistreptococcus serum. Lectures discuss hemotoxins and begin the discussion of humoral immunity and are followed the next week by a consideration of bacteriolysins and hemolysins. Coincidently, the cholera group of spirillæ is being studied culturally, and the action of Buchner's alexin in fresh serum, and of Pfeiffer's specific lysin (Pfeiffer's phenomenon) on *Sp. choleræ* are studied by the entire class. The week ends with class work on the artificial hemolysins and a group preparation of lesions produced by injecting hemolytic (hemotoxic) serum in the animal whose corpuscles were used to produce it. Separate groups of students begin at this time the production of various anti-sera by immunizing animals. This individual work has not only served to familiarize the students with methods of immunizing and bleeding animals, and of testing specific sera, but by modifications has actually suggested ways of perfecting these methods.[2]

The first formal lecture of the seventh week deals with the epidemiology, pathogenesis, and means of specific prevention and therapy in cholera; the second with immune opsonins or tropins. In this and the following week the colon-typhoid group of bacteria is studied culturally, with the logical correlation of class work on the specific agglutinin and precipitin reactions which were first worked out with these organisms. The theoretical and practical aspects of agglutination and precipitation are taken up in lectures.

The work in morbid anatomy and histology in the meantime, after dealing with circulatory disturbance, has taken up diseases of the lung (three exercises) and gastritis (Pearce: Exercise VII, 1, 2, and 3) and by the end of the eighth week is considering the lesions of typhoid fever in connection with the corresponding afternoon work on the typhoid bacillus. At the beginning of the next week amœbic and bacillary dysentery are studied, the latter correlated with a bacteriological study of the main types of *B. dysenteriæ* and rounded out by a second of two lectures on epidemiology, specific immunization, and therapy of infections of the colon-typhoid-dysentery group.

At this point, a week is given to the study of tuberculosis, human and bovine lesions, prepared cultures of tubercle bacilli, staining of tuberculous sputum, injection of guinea pigs with tuberculous sputum and the effect of tuberculin on animals previously so infected. Two lectures deal with the intercommunicability of human and bovine tuberculosis and methods of diagnosis, and specific therapy in the disease. Lesions of leprosy are demonstrated, and the streptothrix group of organisms with cultures are then briefly considered.

The anthrax bacillus and *B. mallei* are then studied for a few days supplemented by a lecture on Pasteur's historical method of anthrax vaccination of cattle, the diagnosis of glanders in horses, and a brief consideration of the two diseases as they occur in animals and in human beings.

The work of the eleventh week deals first with plague and chicken cholera, in the bacteriological hours, supplemented by a study of gross and microscopic lesions of the former disease as it occurs in rats and ground squirrels.[3] A lecture takes up the transmission of plague by rodents and method of preventive inoculation. The week ends with study of cultures of the influenza bacillus and of the bacillus of whooping cough. The morphological work, which at this point shows no particular correlation, deals with diseases of the liver, pancreas, and colon.

The work of the following week groups largely about diphtheria and tetanus. Smears from throat cultures sent to the State Laboratory of Hygiene for diagnosis are studied for the

[2] See Gay and Fitzgerald: The intensive method of immunizing rabbits for the rapid production of antibodies. Preliminary report to appear in the Proceedings of Society for Experimental Biology and Medicine.

[3] I am indebted to Dr. G. W. McCoy of the Public Health and Marine Hospital Service for preparations and tissue from this locally important disease.

presence of diphtheria bacilli.[4] Two or three systematic lectures cover the subject of toxins and antitoxins and the practical aspects of antitoxin preparation and standardization is made clear by a day spent in the Cutter Biological Laboratory. The lesions of diphtheria in human cases are studied and the symptoms and lesions following the injection of diphtheria and tetanus toxin are demonstrated in guinea pigs by individual student groups.

The thirteenth week bacteriologically deals with *B. tetani*, anærobic culture methods, and lesions produced by *B. aerogenes capsulatus* (Pearce: Exercise II, No. 4). In no direct relation the morbid anatomy work is devoted to diseases of the kidney (Pearce: Exercise X). The formal lecture discusses anaphylaxis and is followed by a demonstration of anaphylactic shock in the guinea pig. At the end of the week the lesions of syphilis are studied in conjunction with demonstration of a culture of *Tr. pallidum* (Noguchi), Giemsa and Levaditi preparations, and finally lectures on experimental syphilis and the Wassermann reaction.

Morbid anatomy and histopathology continues for the forenoons of four weeks more and is in no constant correlation with the afternoon work. Tumors are studied for three weeks with an afternoon lecture on the experimental study of malignant tumors in animals. The final week deals with lesions of the central nervous system.

The afternoon work during this period extends from the work on syphilis to a general consideration of protozoan diseases and diseases of unknown etiology. Trypanosomes with smears from an infected rat, blood smears from filaria and malaria occupy one week, with lectures on protozoan immunity and chemotherapy; rabies with diagnostic smears showing Negri bodies is studied in conjunction with a lecture on the subject and demonstration of the action of fixed virus and the preparation of cords for treatment. The tissues of scarlet fever and small-pox with their cell inclusions are studied in conjunction with a lecture on vaccination against small-pox. The practical aspects are reinforced by a second visit to the Cutter Laboratory to observe the methods of preparing vaccine virus.

The last two lectures cover first the diseases of unknown etiology that have been experimentally studied: typhus fever, anterior poliomyelitis, yellow fever, and measles, and last a lecture on the experimental work on cancer. For the last week the student is working with unknown bacterial cultures.

It is believed that a course in pathology such as has been outlined serves best to give the student a clear conception of disease as a general process and of each specific disease as a clearly defined and continuous entity. The method enables him to study the sequence of events as they naturally occur and avoids the suspension of interest that is attendant on courses of bacteriology and morbid anatomy given separately. An attempt is made to deal adequately with functional pathology not only as the logical transition from cause to effect but as a field of greater intellectual and practical importance than either of them.

The actual success of this correlated method of teaching pathology is due largely to the constant suggestion and co-operation of my associates Drs. J. G. Fitzgerald and G. Y. Rusk.

[4] Our thanks are due to Dr. W. A. Sawyer, Director of the State Hygienic Laboratory for these and many other preparations of diagnostic value, particularly in connection with the diagnosis and treatment of rabies, willingly placed at the disposition of our students.

RICHARD BRIGHT'S TRAVELS IN LOWER HUNGARY: A PHYSICIAN'S HOLIDAY.*

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The travels of great physicians have seldom been anything more than matters of casual record, and rarely has a professional man left a detailed account of his journeyings among strange lands and people. We have only a hint or so of Galen's wanderings or of the way in which Dioscorides worked up the data for the first treatise on materia medica while plying his avocations as an army surgeon. Aubrey affords a glimpse of Harvey in Germany, "making observations of strange trees and plants and sometimes like to be lost," and Harvey's own description of his visit to the Bass Rock stands apart as a remarkable bit of impressionistic writing, a sort of Whistlerian "arrangement in white," leaving, even for those who have never seen it, a definite presentment in the mind's eye of the gleaming chalk-white cliffs, coated with crumbled birds' eggs, the myriads of sea-birds and solan geese, whirling and screaming in the June sunlight around the huge rocky pile off the eastern coast of Scotland. In his memorial of Robert Graves, Stokes has left a fascinating account of his colleague's youthful adventures on the continent, his imprisonment as a German spy on account of his suspicious fluency in speaking the language, how he and Turner (the artist) knocked about together for months without asking each other's names, and how, during a storm in the Mediterranean, the high-spirited Graves successfully put down a mutiny on board ship, smashing the life-boat with an axe, overpowering the panic-stricken captain, assuming command over the crew, repairing the pumps with leather from his own boots and successfully bringing the vessel safely into port through his competent seamanship. The Italian travels of John Bell have a special artistic interest; Sir William Wilde's books are eminently readable, and there is interesting matter in the collected letters of Sir Charles Bell, Helmholtz, Billroth and others, not to mention the scathing arraignment of the

* Paper read before the Johns Hopkins Hospital Historical Club, February 12, 1912.

inconveniences and disagreements of Italian travel in the eighteenth century by William Sharpe, one of Bright's predecessors at Guy's Hospital.

But on the whole, it is perhaps not too much to say that Richard Bright's account of his journey from Vienna through Lower Hungary is the most important book of travels written by a physician, for his object in writing it was no less than to give, incidentally, a scientific account of the state of that kingdom at the time of the Peace Congress of 1814-15, just before the close of the Napoleonic wars. The acknowledged master in the special field in which Bright made essay is Sir Richard Burton, and, always excepting the "Pilgrimage" and the African travels, Bright's book, although of an earlier period, will compare favorably with any of Burton's in descriptive talent and scientific accuracy. Like Harvey or Sydenham or Jenner, Bright was the typical Saxon physician and his mind was of a cheerful cast. Humor he had, of the clear-eyed kind which sees things as they are and takes them as they come, but hardly the peculiar twist of phrase which marks the professional or non-professional humorist. There was in his composition not a trace of self-consciousness or whimsicality, nothing of the Celtic habit of saying something funny for its own sake or of that eminently Scotch trait of drawing out other people's peculiarities for private amusement or future reference which Joanna Baillie noted in William Hunter, and which made even his old teacher Smellie somewhat afraid of him.

Few men have entered the medical profession with such a thorough scientific equipment as did young Richard Bright. The son of a Bristol banker, his early years were exempt from struggle and it is not the least interesting trait of his honorable youth that he must have spent it in some hard and exacting study and work. When Sir George Mackenzie visited Iceland in 1810 he asked Bright, then a medical student of twenty-one at Edinburgh, and Dr. (afterwards Sir Henry) Holland to accompany him as experts, "knowing them to be young men of very superior talents and acquirements, in a high degree pleasing in their manners and promising me the hope of numbering them (as I now have the happiness of doing) among my friends." In the volume of travels which resulted from this trip, we find Bright contributing the chapters on the zoology and botany of Iceland, while Holland deals with its literature and institutions and the diseases of its inhabitants. This book is a large quarto volume of the keepsake order, handsome in typography and illustration, published by Constable of Edinburgh, who afterwards printed Bright's Hungarian travels in the same sumptuous style. The author constantly refers to Bright as an ideally cheerful companion who put up with all the hardships and mishaps of the trip with good humor and equanimity. One little contretemps is amusing enough to note in passing. While stopping as guests of Count Trampe, the former governor, the travellers were waited upon at the table by the governor's niece and "an elderly female who had appeared at the same time" and who turned out to be his sister-in-law. "We sent some trifling present to these ladies; and on this account, as soon as we entered the house, it became necessary to submit to the customary salute denoting the gratitude of those who receive presents. On many occasions we could well have dispensed with the ceremony; and our talents were often exercised in contriving means of evasion or escape." More than once, throughout this Icelandic itinerary, we have the diverting spectacle of three able-bodied, hard-headed young men at infinite pains to dodge the country schoolboy's nightmare of being "honey-fugled with a righteous kiss."

In the year 1841 Dr. Bright, then a young man of twenty-five, sometime an interne at Guy's and a recent graduate from Edinburgh, took a long vacation tour on the continent, incidentally attending lectures and clinics at Berlin and Vienna. In the winter of 1814-15 we find him back in London again, studying skin diseases at Bateman's clinics, a subject in which he and Addison always had a keen interest. In March and April, 1815 he made his two journeys into Hungary, returning home through Belgium, shortly after the battle of Waterloo, where he saw many interesting cases. The result of his continental travels was a large quarto published by Constable in 1818, with interesting illustrations all the work of his own pencil, ten of them engraved by different hands, the rest clever wood-cuts. His narrative begins with two chapters descriptive of Vienna, whither he had come to see the Peace Congress then in session. He arrived there toward the end of November, and his first lodging was "a busy and dirty inn in the commercial part of the city, which was much frequented by Greeks, Armenians and Eastern merchants." His apartment he describes as "large and desolate, without a carpet, but provided with an earthen stove in one corner, and a little wooden bedstead in the other. Such are the miserable accommodations in most of the inns at Vienna." He immediately set forth on a tour of investigation, finding the narrow streets, on a level with the carriage ways, so risky of access that "the foot passenger has no safety but in the judgment of the charioteer, who frequently risks an encounter with your feet, rather than with the wheels of a passing carriage. The coachmen, however, give some warning of their approach, by a species of unintelligible roar, a little in accent like the language in which a Lancashire carter converses with his team; but not less peremptory than the rapid 'by your leave' of a Bath chairman." Returning at an early hour he goes on, "I retired to the box, for it deserves no better name, which was destined to receive my weary limbs." Next morning he was awakened by a succession of visitors, characteristic of the Vienna of those days, a chiropodist, barber, female tooth-brush vender, and two turbaned sellers of meerschaum pipes; having disposed of these, he settled down to a breakfast "consisting, as is usual in Germany, of a jug of hot scalded milk and another of coffee." It is Sunday, a day of festivity as well as of piety in Vienna, and he is advised to go to the *Redoute* in order to see the exalted personages of the congress. Entering the Hofburg he finds himself in a brilliantly lighted salon of splendid dimensions, and we are now in the full swing of his narrative.

> Never was an assembly less ceremonious; every one wore his hat; many, till the room became heated, their great-coats; and no one pretended to appear in an evening dress, except a few Englishmen. . . . Around the whole circumference of the room

were four or five rows of benches, occupied, for the most part, by well-dressed females; while the other parts presented a moving multitude, many of whom were in masks, or in dominos, and were busily engaged in talking and laughing, or dancing to the music of a powerful orchestra. My companion squeezed my arm, as we passed a thin figure with sallow shrunken features, of mild expression, with a neck stiff, bending a little forwards and walking badly. "That is our Emporor." I shook my head and smiled. . . . "There, do you see that little man with white hair, a pale face. and aquiline nose? He was almost pushed down as he passed the corner. That is the King of Denmark." Again I shook my head in disbelief. "Here the Emperor of Russia approaches." I looked up, and found the information true. His fine, manly form, his round and smiling countenance, and his neat morning dress were not to be mistaken; they were the same which, some months before, I had seen enter the church at Harlem, to the thundering peals of the grand organ. I soon recognized the tall form, the solemn and grave features of the King of Prussia. . . . "That was the Grand Duke of Baden," said my monitor, "whose toe you trod upon. . . . See, three women in masks have beset the King of Prussia; he seems not a little puzzled what he shall do with them. . . ." "Who is this young man next to us, marked with the small-pox, who is speaking broken English?" "It is the Crown Prince of Bavaria; he is said to be very fond of your nation. . . ." After a little more pushing, for the room was now becoming very full, we encountered a fine, dark, military-looking man, not in uniform, of course, but with moustaches. This was Beauharnois, viceroy of Italy.

Returning home at a late hour in the morning Bright succeeded in changing his lodging and went on with his round of sightseeing. In the grand square in front of the Hofburg he heard the sentinels announce the approach of royalty by "a yell more hideous than ever issued from the mouth of a Cherokee Indian," set off by a flourish of rolling drums. At the Carrousel he saw the splendid tournaments "contrived to dissipate the ennui of royalty" by the nobility, which consisted in riding full tilt at dummy Turk's heads (a natural object of Viennese aversion) and sweeping them off, one after another, by successive saber-strokes. Of the gorgeous uniforms of the participants he observes that "they bore the appearance of being the substantial fruits rather than the honorable testimonials of victorious arms"; and he notes that the congress was, in general, disappointing, since its splendor was entirely that of the Austrian Court, with little display on the part of the foreign visitors. He describes the Viennese picnics, tableaux, charades, dinner parties, the street scenes in Old Vienna, the crowds in the Prater, the religious ceremonials, the theaters and the innumerable court balls, concerning which one of the participants formulated an epigram which sounds like a premonition of the Old Guard at Waterloo: *le congrès danse, mais il n'avance pas.*

During his stay in Vienna Bright paid a special visit to Schönbrunn, where Marie Louise was then living in seclusion; he was taken in to see her infant son, and this is his impression of *l'Aiglon:*

He was the sweetest child I ever beheld; his complexion light, with fine, white silky hair falling in curls upon his neck. He was dressed in the embroidered uniform of a hussar, and seemed to pay little attention to us as we entered, continuing to arrange the dishes in his little kitchen. I believe he was the least embarrassed of the party. He was rather too old to allow of loud praises of his beauty, and rather too young to enter into conversation. His appearance was so engaging, that I longed to take him into my arms, yet his situation forbade such familiarity. Under these circumstances, we contrived a few trifling questions, to which he gave such arch and bashful answers as we have all often received from children of his age, and, after a few minutes conversation with Madame Montesquieu, we withdrew.

At the time of Bright's visit the Old Vienna School—Van Swieten, Auenbrugger, Stoll, de Haen—had long since passed away, and the members of the New Vienna School—Semmelweis, Hyrtl, Hebra, Skoda, Rokitansky—were either unborn, in their infancy, or in their teens. The sole survivor of the Old Vienna School was Johann Peter Frank (1745-1821), who, at time of Bright's visit, was the leading medical man of Vienna and in our own time enjoys the distinction of being the first physician to emphasize the importance of diseases of the spinal cord, while his "Complete System of Medical Polity" (*System einer vollständigen medicinischen Polizei*) is, if we except the thirteenth and fifteenth chapters of the Book of Leviticus, the true foundation of public hygiene. This remarkable work, which contains in theoretical solution all those hygienic problems which are words of ambition to-day, such as the medical inspection of schools, proper food and suitable benches for the school children, even the taxing of bachelors, was published as far back as 1777 by Schwann of Mannheim, the printer of Schiller's "Robbers." Its author, a rare and happy combination of French intelligence and German thoroughness, made his way up from obscurity to become one of the great figures of German medicine by his own unaided industry. As with Schiller, his early life was the scene of privation, struggle and parental harshness—

Der Sorge Wohnsitz die den blonden Knaben
Früh lehrte. wie man duldet, kämpft, entbehrt—

but Bright gives us a pleasing glimpse of a kindly old gentleman at ease, and at peace with himself in the evening of his life, receiving the unknown English youth with consideration and urbanity. "He is a man of the most instructive and pleasing conversation, with great knowledge both of books and men, and is most universally respected. He is now above seventy years of age, is perfectly firm and upright, and, in all his faculties and dispositions, possesses the force and energy of youth, tempered by the mildness of advancing years."

The general state of science in Vienna Bright describes as far from flourishing, by reason of the difficulties and obstacles placed in the way of education, the narrow-minded censorship of the press and of foreign publications and the relatively small number of scientific men. Besides Frank, the most notable of these were Hildenbrand, memorable for his early work on typhoid fever (1810), the ophthalmologist Beer, Vincenz von Kern the surgeon, who revived the cold water bandages of Cesare Magati (1616) as a simple treatment for wounds, and the anatomist Prochaska, whose studious secrecy and mercenary disposition in regard to a certain method of injecting anatomical preparations are duly deplored by our author.

Prochaska is ready, for fifty ducats, to supply to the curious small cabinets, accompanied with a microscope, and containing

about seventy microscopic specimens, showing the most minute ramifications of different vessels in the various structures of the body. It appears that this art of subtle injection is the same which Lieberkühn employed before them, and which was lost after his death. It would, indeed, be a blot upon the scientific spirit of the university of Vienna, if a second time such a discovery should be suffered to perish.

Of Hildenbrand Bright says:

This very able physician is the worthy successor of the celebrated Stoll and Frank; he devotes himself very assiduously to the improvement of the students, whose education, in the practical parts of medicine, he superintends. He visits the patients, in company with the pupils, as early as seven o'clock in the morning, and afterwards delivers a very excellent course of medical lectures in Latin.

De Carro, who was educated in England, at least deserves remembrance as the pioneer of Jennerian vaccination, both in Europe and in Asia, beginning his experiments, like Benjamin Waterhouse, upon his own children (1799). Count Harrack is praised by Bright for a variety of philanthropy which, except in the case of Émile Littré, is not on record as an exclusive feature of medical practice.

This singular man turned his attention to the study of medicine somewhat late in life, for the sole purpose of doing good, and continues to spend his time unceasingly in relieving the miseries of those who are unable to make pecuniary return for the attentions and advice they receive. This species of benevolent exertion is much needed in Vienna, where there are none of the smaller medical charities and dispensaries, which abound in our own country.

It appears that Count Harrack even attempted to memorialize the Peace Congress to induce the Sublime Porte to set aside religious prejudice in checking the ravages of plague in Turkey, but, very naturally the project fell through, and as Bright quaintly observes, "the followers of Mahomet still continue to view the plague with superstitious resignation."

Before leaving Vienna we may note Bright's description of the famous *Narrenthurm,* or "Lunatic's Tower," erected in 1784, one of the show places of Old Vienna, where, as in ancient Bedlam, the public were allowed to view the insane, like animals in a menagerie, on payment of a small fee.

The Asylum for the Insane is a fanciful edifice, and not well contrived. Externally, it appears a large round tower; and, on entering, it is found to consist of a hollow circle, in the center of which a square building rises, joined to the circle by each of its angles. The circular part contains the patients, and the inclosed building is intended for the residence of the keepers and the surgeon. This building is four stories high, besides the ground floor . . . . It contains 300 patients, whose condition is far from being as comfortable as in many of the establishments for the insane which I have visited.

In March, 1815, Bright, amply provided with letters of introduction to Hungarian nobles, set out from Vienna for Pressburg, journeying eastward through the flat, open country along the right bank of the Danube, and finding little of interest until he arrived at the estate of a hospitable magnate who bore the name of Count Hunyadi. The Graf, as Bright styles him, was away from home, but the director of the estate soon assured the traveller that it was an essential part of Hungarian hospitality to receive an honored guest with the same ceremony as if the master were present. Here he remained for several days and then proceeded to the silver mines of Schemnitz, in the Carpathian Mountains, and thence to Buda Pest, returning westward to Vienna by way of Raab. His second trip, in April, 1815, was another circular tour, southward from Vienna to the Balaton Lake, passing along the borders of Croatia to Fünfkirchen, then northward again to Buda Pest, returning eastward through Styria. In this way he saw the fringe of the Puszta, but did not get across the Danube into Transylvania.

In such an extensive itinerary, occupying some six hundred pages, we can best appreciate Bright's narrative by considering the things which excited his greatest interest. First of all, the people. Of Bright's very human descriptions of the Hungarian nobles and their vassals, we may say, as George Moore said of Turgenieff, that he judged both gentleman and peasant "as a scholar and a philosopher, without small-beer cynicism or that air of which Thackeray could never divest himself, of having been in society after the success of one of his books." His artistic eye delights in minute notations of the differences in female costume—Hungarian, Sclavonian, Styrian, Wallachian, Illyrian—and he devotes page after page to an endeavor to make the reader understand the almost medieval status of the Hungarian peasant at the beginning of the nineteenth century. His conclusion is that "it is not only in appearance, but in reality, oppressive. The appearance of oppression constantly imposing on the sufferer a consciousness of his humiliation, is of itself an evil hard to bear," but, even if the master were kind, the harsh condition imposed by the government itself, the heavy tolls and tributes, the quartering of troops, the constant labors required in road-making, bridge-building and other public works, made it impossible at this time for the peasant to reap any just reward for his labors.

It is certain that the whole system is bad. . . . A man of capital can bear, for a year or two years, the failure of his crops; but, let a cold east wind blow for one night—let a hailstorm descend—or let a river overflow its banks—and the peasant, who has nothing but his field, starves or becomes a burthen to his lord.

Of the peasants themselves he says:

They were cheerful—but it was the cheerfulness of boys under the eye of their master—and there was something disagreeable in that appearance of timorous, yet rebellious, subordination, which seemed to say—"This is hard—but it must be so. . . ." No one can remain long in Hungary, without seeing that all who are in stations superior to the peasant look on him with contempt, mingled with suspicion and dread.

In regard to one detail of Hungarian feudalism, a survival of the ancient Jus Gladii, or right of the lord to inflict capital punishment or imprisonment upon his serfs, our author rises almost to indignation, held in restraint by the fact that he was speaking of his hospitable hosts.

The traveller seldom approaches the house of a Hungarian noble, who possesses the Jus Gladii, without being shocked by the clanking of chains, and the exhibition of these objects of misery loaded with irons. The prison itself is never concealed from the curiosity of strangers; I should almost say that it is considered a boast—a kind of badge of the power which the lord possesses. . . . It is scarcely credible, that men of the noblest and most refined minds, should persist in the barbarous custom of placing in the

very gateway of their hospitable mansions—in the only path by which their offspring can approach the domestic hearth—the miserable victims of a most sacred, but, at the same time, most painful and revolting duty.

Bright differentiates clearly between the Slavic (Slovak) and Hungarian peasant, and in respect of neatness and cleanliness, very much to the advantage of the latter. Of the Sclavonian peasants he says:

When you have seen one you have seen all. From the same little head, covered with oil, falls the same matted long black hair, negligently plaited or tied in knots; and over the same dirty jackets and trousers, is wrapped on each a cloak of coarse woolen cloth, or sheep-skin still retaining its wool. Whether it be winter or summer, week-day or sabbath, the Sclavonian of this district never lays aside his cloak, or is seen but in heavy boots.

Add to this the fact that many were afflicted

with that unseemly disease, known by the name of Plica Polonica, in which the hair grows so matted that it is impossible to disentangle it, and becomes actually felted into balls, which, from an unfounded apprehension of bad consequences, the peasants are very unwilling to have removed. . . . The real Hungarians showed far greater attention to personal neatness, and like the gypsies, were often dressed in hussar jackets, blue pantaloons, boots and broad-brimmed hats, which gave them the appearance of banditti.

This appearance often merged into reality in the open country, through their characteristic love of indolence and the passion for wild life and freedom. As in old days on the Scotch border, "the herdsmen are usually mere thieves, stealing cattle when they are able." Bright found the Hungarian gypsies singularly like those at home, not only in appearance but in language. He made an extensive vocabulary of gypsy words, and, when he got back to England, one of the first things he did was to look up a family of hedge-gypsies at Norwood, to find to his delight that they recognized almost every word he could recall. Like George Borrow, he speaks with lively sympathy of the advantages of the free, independent roaming life of these people in the open air.

I leave it to those who have been accustomed to visit the habitations of the poor in the metropolis, in great cities, in country towns, or in any but those Arcadian cottages which exist only in the fancy of the poet, to draw a comparison between the activity, the free condition, and the pure air enjoyed by the gypsy, and the idleness, the debauchery, and the filth in which a large part of the poorer classes are enveloped.

Bright was an early advocate of the view that the gypsies, Tzigani or Egyptians, were originally a nomadic Hindu tribe, and, in support of this contention, he cites an interesting verse from old Skelton, descriptive of the Oriental turban worn by Elynoure Rumminge:

Her kirtell Bristowe red,
With clothes upon her heade,
That they way a sowe of leade,
Wrythen in a wonder wise,
After the Sarazins gise,
With a whim wham
Knit with a trim tram
Upon her brayne panne,
Like an Egyptian
Capped about
When she goeth oute, &c.

In seeking contact with the Hungarian peasants and gypsies, Bright naturally found opportunities to see their national dances and hear their music, and he describes a concert which was improvised in his honor at a gipsy farmhouse, as follows:

A Cygany woman sat upon the projecting part of the heated stove, and spun with a distaff while the children crowded behind her. The four musicians arranged themselves in a circle, and a few peasants who entered, made up the party within doors. . . . The instruments were three violins and a violoncello, and, at my request, the tunes they played were the national airs of the Hungarians and Sclavonians. After listening for an hour, I was not sorry to bring the concert to a conclusion; for in truth the room, with its low boarded roof, was but little calculated for such a powerful band.

In the theaters at Buda Pest, Bright was especially attracted by the musical instruments, one of which, a set of strings struck by a plectrum, resembled the *Langspiel* which he saw in Iceland. Another was the *Dudelsack,* or Hungarian bagpipe; and a third, the cymbalom, or *Glockenspiel,* which he thought of Turkish origin.

A subject in which Bright took a curious interest was the burial of the dead. Of a deeply religious nature himself, he seems to have regarded the emotions displayed at funerals as a test of sincerity, and he attended several, he says "as a ceremony which no one ought to neglect in a foreign country." One of the finest traits of old-fashioned German character is (or was) the deep reverence and regard of children for their parents. Of this, he gives a touching example:

When I was at Berlin, during the preceding year, I followed the celebrated Iffland to the grave. Mingled with some pomp, you might trace much real feeling. In the midst of the ceremony my attention was attracted by a young woman, who stood near a mound of earth newly covered with turf, which she anxiously protected from the feet of the pressing crowd. It was the tomb of her parent; and the figure of this affectionate daughter presented a monument more striking than the most costly work of art.

The following may be taken as an expression of his views on the subject of religion:

These humble peasants of Hungary have, through the native promptings of the heart, so blended the memory of their departed friends with the feelings of devotion, that nations boasting of higher degrees of cultivation may respect and follow their example. We may civilize and refine away our feelings till the simple dictates of nature are completely yielded up. With the majority of mankind consolation is sought in forgetfulness. . . . If, putting aside all unintelligible motives, there is one which can be felt and explained, more pure than others, leading us to rejoice in our future prospects, it is the idea and hope of meeting again the friends from whom we have been separated by death.

On the road Bright's journey through Hungary was, in a sense, "roughing it." He usually travelled in a rough peasant's wagon, the wheels of his conveyance sinking "to their naves" in the mud of the boggy roads, encountering languages, as Henry James puts it, "perceived to be foreign but not further identified," so that his conversation with the toll-gate keepers and other roadside officials was, of necessity, in Latin. It was often impossible to get transportation or change of horses without a special order, and sometimes the postillion would unload him at an impossible inn, with fair promises of the best accom-

modation, and, while he was inside, would seize the occasion by the forelock and beat a hasty retreat. The fear of banditti was another excuse for shilly-shallying, and, on one occasion, when "a very exorbitant and unmanageable postmaster" gave this as a reason for avoiding the main road and taking a circuitous route, "the matter was settled, and all the banditti put to flight, by my agreeing to his terms, and paying a heavy extra charge." At the roadside hostelries, his sensations were scarcely those of the idealized eighteenth-century traveller, who,

> Where'er his stages may have been,
> May sigh to think he still has found
> His warmest welcome at an inn.

He had what were the common experiences of travellers in Eastern Europe at that time.

The most interesting feature of Bright's visit to Buda Pest is his account of the medical institutions. At this time, the University was frequented mainly by Hungarians and Transylvanians, young men who, in earlier days, sought an education in Germany or Italy. The lectures were delivered in Latin, and it is of interest to note, in this connection, that while Cullen, about the middle of the eighteenth century, had already begun to lecture on medicine in English, it was not until the advent of Schönlein at Berlin, in 1840, and of Frerichs at Breslau in 1851, that medical lectures were delivered in German. The medical course at Buda Pest extended over five years, and is outlined by Bright as follows:

First year.—Anatomy, chemistry, botany, natural history, general pathology, and surgery.

Second year.—Physiology, more minute anatomy, the theory of operations, surgical instruments, and midwifery.

Third year.—Pathology, materia medica, and diseases of the eye.

Fourth year.—Therapia of acute and chronic diseases, with clinical lectures both in medicine and surgery; and lastly, the veterinary art, which, however, may be postponed till the fifth year, or till the course is completed, but must be pursued before a diploma can be granted.

Fifth year.—The particular therapia and the clinical studies are continued, to which are added, medical jurisprudence and medical police.

The University Hospital at Buda Pest consisted of several wards of six beds each, one each for medical, surgical, and gynecological cases, one for diseases of the eye, one for lying-in women and one for syphilis. Another ward was wisely set apart for the instruction of young surgeons in internal medicine. The fourth and fifth year students attended the patients in the different wards, and each was required to report his cases in Latin and to make a separate monthly report of everything he had seen. One special duty of the pupils was to keep "a thermometrical and barometrical register," and these studies in medical meteorology, a distant reflex of the influence of Sydenham, were regularly checked up from observations made by the professor of astronomy.

He goes on:

I was much pleased with the order and regularity with which this hospital is conducted, and am not sure that more celebrated institutions might not gather hints from the proceedings of this distant and almost unknown medical school. It must, however, be owned that the whole is more manageable from its small extent, as there were not above eleven students in their fourth and fifth years, nor above thirty in the earlier years of their medical studies.

With the exception of Kitaibel, who showed Bright through the hospital, there were no medical men of consequence in Buda Pest at this time. But Hungary has given to medicine some unique names: first and foremost, the noble, self-sacrificing Semmelweis; the almost forgotten Stephan Weszpremi, whose *Tentamen de inoculanda peste,* published in London in 1755, outlined a plan of preventive inoculations against the plague; Hyrtl, the anatomist and Mikulicz, who described a new form of disease (simultaneous inflammation of the parotid and lachrymal glands) and was one of Billroth's most brilliant pupils; and, in more recent times, Robert Barany, who, only the other day, in his clinic at Vienna, went far towards clearing up the hazy subject of Menière's disease by showing, through successful operations on the internal ear, that the rotary movements, nausea and dizziness obtained by having a patient point at an object with eyes shut after previously touching it constitute a true index of labyrinthine affection (vestibular nystagmus).

While in Buda Pest, Bright paid several visits to the public warm baths of the city, many of which, he says, were "very ancient buildings, some supposed to be of Roman, others of Turkish construction." His impressions of the public baths, evidently frequented by those in the lower walks of life, may be summed up in the early Victorian epithet—Shocking! The interest of his very realistic description is that it tallies exactly with what we see in the pictures of the sixteenth century artists, Lucas Cranach, Hans Sebald Beham, Aldegrever, Hans Bock and the rest of the German *Kleinmeister.*

On entering from the open air, the room, filled with steam, was so insufferably hot, as almost to oblige us to retire. In addition to this, it appeared dark; but in a few moments both our bodies and eyes became accustomed to their new situation. The apartment was spacious, the center being occupied by a circular basin under a dome supported by pillars. The descent into this is by two steps ranging round the whole of its circumference. Here we beheld ten or twenty persons of each sex, partially covered with linen drawers and the long tresses which fell loosely from their heads, amusing themselves by splashing in the hot sulphurous water. Disgusting as this was, it formed the least disagreeable part of the scene. On the outside of the pillars, the floor was paved, and there lay, at full length, numerous human creatures, indulging, amidst the fumes, a kind of lethargic slumber; others lay upon the steps, and submitted to the kneading practiced upon them by old women employed for the purpose; some, as if resting from their labors, lay stretched upon benches; and in different corners were groups of naked families, enjoying their mid-day meal, sour crout and sausages, amidst all the luxury of a profuse perspiration. To complete the scene, there was a row of half-naked figures, like those in the bath, on whom a poor miserable surgeon was practicing the operations of cupping and scarification, studiously inflicting wounds, and making as much show of blood as possible, in order to satisfy the immoderate appetite of the Hungarian peasant for this species of medical treatment. With such a mixture of disgusting objects it never before happened to me to meet, and, almost faint with heat, I was glad to make my escape; yet my curiosity led me to several others; but in none was the construction of the chamber so

picturesque. The enjoyments of the baths, however, were the same.

Even as a youth of five and twenty Bright was a man of extraordinary thoroughness, with an almost Germanic passion for classification and tabulation, and his mind saw everything in categories. One instance of this will suffice, his synopsis of the course of instruction for women at the Georgicon or public school on the estate of Count Festetits—a relic of pre-suffragette days which bears the superscription:

Objects of Female Industry.

In the first year. 1. Plain and ornamented knitting, the commencement of the sampler. 2. Hemming and seaming, quilt stitch, overcasting, and Hungarian sewing. 3. Music. In this year the pupils are expected to produce a pattern piece of knitting, a sampler, a plain knit stocking, a child's cap, and a shirt.

In the second year. 1. Continuation of the samplers, knitting a common frock for a child, and an open-work cap; together with clothing and gloves. 2. Sewing a pillowcase with buttonholes, sewing a shirt and a pair of drawers and a fine shirt with frills. 3. Spinning on the wheel. 4. Care of silk-worms and the winding of silk. 5. Music.

In the third year. 1. Fine stockings with clocks; lace-making; a lace cap and a purse; knitting a woman's cap. 2. Sewing a great coat with lace; sewing women's clothes and corsets; cutting out and practice in making up caps. 3. Washing, plaiting and ironing. 4. Drawing, as connected with female work. 5. Cooking, and other economical employment. 6. Music.

We will leave the scene of Bright's travels with a parting glance at the Hungarian enjoying his lazy gypsy life in the sunshine:

If any thing could show a want of reason, or of domestic connection and civilization, it was these groups of men, not with their families—not with their wives—not in conversation with each other—but herding together, merely because the same sloping bank invited each of them to the enjoyment of basking in the sunbeams. There they might be counted by tens, stretched out at length, wrapped in greasy sheep skins, and dreading the trouble of entering the church, where the priest had already begun to read the prayers. Arriving upon the borders of a forest, my companion quitted me, and I proceeded alone. The day was delightful; the forest was chiefly birch; the flowers were richly spread upon the ground; and I was surrounded by blackbirds and nightingales in full song. I saw two or three fine green, and several grey lizards, enjoying themselves in the warmth of the sun.

It has been a matter of comment that this Hungarian journey was of immense value to Bright in after life, in that the experience increased his faculty of vision and sharpened his powers of observation, while in the record itself he had already perfected his gift of literary expression. The style, at times a little ornate and stilted to moderns perhaps, yet still, as Lowell said of Washington, "the habitual full-dress of his well-bred mind," is a remarkable achievement for a young man of twenty-five.

The illustrations in Bright's book, his own handiwork, will go far to show that his genius as a clinician was of a piece with this priceless artistic faculty. Long afterwards, at Guy's Hospital, Wilks observed that "Bright could not theorize, but he could see." Stevenson once said of a prospective traveller: "Tell him it is the mark of a parochial gentleman who has never traveled, to find all wrong in a foreign land. . . . Let him resist the fatal British tendency to communicate his dissatisfaction with a country to the inhabitants. 'Tis a good idea, but it somehow fails to please." These random notes will have failed of their object if they presented Bright as other than an ideal traveller in this respect. It is true he grumbles a little more here and there about his indifferent lodgings, as most of us would, and his ethical sense is aroused by the sorrows of the peasantry; but the hardest things he has to say are usually about his own country, and the extension of his sympathy to objects so remote has all the attractive self-surrender of youth. He puts up with the boggy roads, the squalid hovels, the wretched accommodations, the ignorance and indifference of the natives with supreme good temper and that Saxon strain of humor which consists in mantaining an attitude of extreme gravity or self-possession in the face of almost any queer thing that may happen. Even as a young man, Bright never steps out of his dignified rôle to be consciously humorous, but a few sentences here and there may show his manner of dealing with a humorous situation. Passing through the Hungarian countryside, he observes that "Nature had done much in forming a strong race of men, however deficient the cattle may be in beauty or size"; and, in another place "As the carriage passed, the men bowed respectfully; the salutation of the women was less discernible." It was his ambition to write a special chapter on the Hungarian literature, but he soon found, for Hungary (as for our own country) in the year 1815, that as the March-Hare said to Alice in Wonderland, "There isn't any."

Bright paid another visit to the continent in 1818, spending some time in Germany, Switzerland, Italy and France, but his time for writing travels was over and he was now settling down to the serious business of his life. He commenced private practice in 1820, after passing through an almost fatal attack of fever in connection with his duties as assistant physician at the London Fever Hospital, and in the same year he accepted a similar post at Guy's Hospital. He became an F. R. S. in 1821 and in 1824 was appointed full physician at Guy's, Addison having been made assistant physician at the same time. Three years later he published the work which was to make his name famous all over Europe, the first of the two splendid volumes of "Reports of Medical Cases" (1827), elaborately illustrated with full-page plates from water-color drawings, and, apart from its scientific interest, a unique monument of that sportsmanlike devotion to their profession which so many physicians have shown in a field of literary venture which is costly but never remunerative. In 1832 Hodgkin published his original paper "On Some Morbid Appearances of the Absorbent Glands and Spleen";[1] and in 1855 Addison's book "On the Constitutional and Local Effects of Disease of the Supra-renal Capsules" appeared, his preliminary communication on the subject having been read before the South London Medical Society in 1849.[2] Bright's disease, the original correlation of inflammation of the kidneys with dropsy and

[1] Med. Chir. Tr., Lond., 1832, XVII, 68-114.
[2] Lond. M. Gaz., 1849, XLIII, 517.

albuminuria, immediately made its fortune, as the French say, on account of its immense importance in medical practice. The discoveries of Hodgkin and Addison were slurred over as mere curiosities, and although we find Virchow reporting upon Addison's disease and upon the chemistry of the suprarenal capsules in 1857,[3] it was due to the equity and loyalty of Sir Samuel Wilks, the zealous, but not jealous, guardian of the honor of Guy's Hospital, and to the fair-minded and generous Trousseau, that these diseases were given their permanent place in modern medicine.

The remarkable original work done at Guy's Hospital is properly a subject for the pathologist and the clinician, but it may be worth while in passing to glance at these discoveries from the bibliographic angle in their historic sequence, particularly as a flood of light has been shed over the whole matter in the "Biographical Reminiscences" of the late Sir Samuel Wilks (1911). It was here that Sir Astley Cooper did some of the earliest work in experimental surgery after the time of John Hunter (1836);[4] here Addison, Golding Bird and Gull first tried the effects of static electricity in disease (1837);[5] here Pavy did his first experimental work in diabetes (1853);[6] here John Cooper Forster performed the first gastrostomies in England (1858-9);[7] and here occurred what might be regarded as an event in the history of obstetrics, the first findings of albuminous urine in cases of puerperal eclampsia by Lever in 1843,[8] the most important outcome of Bright's teaching in albuminuria. But the special achievement of the men of Guy's was in the department of original descriptions of disease.

The eighteenth century was especially rich in new descriptions of diseases, many of which, as Friedrich Hoffmann's account of rubella (1740), Watson's description of scleroderma (1754), Robert Whytt on tubercular meningitis (1768), Sœmmerring's case of achondroplasia (1791), or John Haslam's account of general paralysis (1798), have only been brought to the front in recent years. In the first quarter of the nineteenth century, we have Otto's description of hæmophilia (1803), Vieusseux's sketch of cerebro-spinal meningitis (1805), Badham's little book on bronchitis (1808), Hildenbrand on typhoid fever (1810), Bayle on phthisis (1810), Wells on rheumatism of the heart (1812), Sutton on delirium tremens (1813), Blackall and Wells on albuminuria (1814), Hodgson's book on diseases of the arteries, containing his account of dilatation of the aortic arch (1815), Parkinson on paralysis agitans (1817), Bostock on hay fever (1819), Bouillard's description of aphasia (1825), Louis on phthisis (1825), and Bretonneau on diphtheria (1826). Laënnec, in the first and second editions of his treatise on mediate auscultation (1819-23), aside from his classical pictures of bronchitis and pneumonia, described and differentiated almost every pathological occurrence inside the chest—bronchiectasis, pneumothorax, hæmorrhagic pleurisy, gangrene of the lungs, emphysema of the lungs, œsophagitis, and one form of cirrhosis of the liver. Sir Clifford Allbutt refers to "the spacious times of Bright and Addison," and there was indeed a mighty sweep to the clinical work of these two men which can only be paralleled by what Laënnec and Louis, Corvisart and Bouillaud, were doing across the channel, or in some measure by the work of Graves, Stokes and the physicians of the Irish school.

The physicians of those days had no instruments of precision except their five senses. Even as late as 1870, Wilks tells us the clinical thermometer was considered a curiosity at Guy's and Dr. Weir Mitchell points out that it was "under the influence of the great Dublin school, that the familiar figure of the doctor, watch in hand, came to be common-place."

Bright's economy of means in testing urine for albumen, only a candle and a spoon, reminds us of Virchow cutting sections all his days with an old every-day razor, or of Sharpey demonstrating kymographic tracings to his class with the aid of a rusty, well-worn beaver hat as a cylinder.

In addition to the diseases called by their names, Bright, as far back as 1833,[9] had described cases of pancreatic diabetes and pancreatic steatorrhœa, and is to be credited with early accounts of acute yellow atrophy of the liver (1836),[10] unilateral convulsions or Jacksonian epilepsy (1836),[11] and acute Hodgkin's disease or "status lymphaticus" (1838).[12]

Addison, in 1849 (London, M. Gaz., 1849, XLIII, 517), twenty years before Biermer, described acute pernicious anæmia, and in 1851 (Guy's Hosp. Rep., 1851, 2. s., VII, 265), with Sir William Gull, the skin disease known as xanthoma (vitiligoidea); and Hodgkin described aortic regurgitation in 1827 (Lond., M. Gaz., 1828-9, III, 433-443—read before Hunterian Society, February, 1827), five years before Corrigan's classical paper was published. In 1856 Sir William Gull (Guy's Hosp. Rep., 1856, 3. s., II, 143) gave perhaps the earliest account of the degenerations of the posterior columns of the spinal cord in the locomotor ataxia, and in 1873 described myxœdema (Tr. Clin. Soc. Lond., 1873-4, XII, 180-185), to which Ord gave the name in 1877 (Med. Chir. Tr., Lond., 1877-8, LXI, 57-83). Finally, Sir Samuel Wilks himself made important and elaborate studies of Bright's, Addison's and Hodgkin's diseases, to the latter of which he gave the name in 1865, described linear atrophy of the skin (lineæ atrophicæ) in 1861 (Guy's Hosp. Rep., Lond., 1861, 3. s., VII, 297-301), necrogenic (dissecting-room) warts ("verrucæ necrogenicæ") in 1862 (Ibid., 1862, 3. s., VIII, 263-265), published one of the earliest papers on visceral syphilis in 1863 (Ibid., 1863, 3. s., IX, 1-64, 4 pl.), and, in 1869, gave interesting accounts of the external manifestations of osteitis deformans (Tr. Path. Soc., Lond., 1868-9, XX, 273-277) and acromegaly (Sir S. Wilks, Biographical Reminiscences, Lond., 1911, pp. 188-189). Perhaps the most important original contribution which Wilks made to medicine was the description of alcoholic paraplegia in his lectures of 1868 (Med. Times & Gaz., 1868, II, 470), which, as Osler points out (New York Med. Jour., 1904, LXXIX, 570), "was the foundation of English teaching on the subject, and, as describing the mental symptoms, contains all that is implied in the useless eponym "Korsakoff's insanity." Even as far back as 1786 Lettsom, in what is perhaps the earliest paper on the drug habit (Mem. Med. Soc., Lond., 1779-87, I, 128-165), had already outlined the pathological effect of alcoholism. The cases of priority discussed by Wilks are of little importance in relation to the time of their publication but are of unusual interest in confirmation of well authenticated modern discoveries. In the same sense, Velasquez's dwarfs, the pictures of rhinophyma by

[3] Deutsche Klinik, Berl., 1857, 441, and Virchow's Arch., 1857, XII, 481.

[4] Guy's Hosp. Rep., Lond., 1836, I, 457, 654.

[5] Ibid., 1837, II, 493.

[6] Guy's Hosp. Rep., Lond., 1853, 2. s., VIII, 319.

[7] Ibid., 1858, 3. s., IV, 13; 1859, V, 1.

[8] Ibid., 1843, 2. s., I, 495.

[9] Med. Chir. Tr., Lond., 1833, XVIII, 1-56 (Case 1).

[10] Guy's Hosp. Rep., Lond., 1836, I, 604-637.

[11] Ibid., pp. 36-40.

[12] Guy's Hosp. Rep., 1838, III, 437.

RICHARD BRIGHT.

PORTRAIT OF BRIGHT, PAINTED BY T. R. SAY.

MARKET AT BATHS.
(Original Drawing by Bright.)

Ghirlandajo in the Louvre and by the younger Holbein in the Prado, or Lucas van Leyden's portrait of Ferdinand I. of Spain in the Uffizi, giving the "adenoid face," might be regarded as instances of priority, antecedent to Romberg, von Hebra, or Wilhelm Meyer.

In the case of Bright, as Wilks said, "we are struck with astonishment with his powers of observation, as he photographed pictures of disease for the study of posterity." In the introductory address to his classes for the year 1832, there is an often quoted sentence which is a remarkable example of his power of visualizing these things:

By the EYE you will learn much; many diseases have the most distinct physiognomy. The sunk and shrivelled features derived from the long-continued disease of the abdominal viscera, the white and bloated countenance often attendant on changes in the functions or structure of the kidney, the sallow and puffy cheeks of the liver diseased from habitual intemperance, the squalid and mottled complexion of the cachexia dependent upon the united effects of mercury and syphilis, the pallid face of hæmorrhage, the waxen hue of amenorrhœa, the dingy whiteness of malignant disease, the vacant lassitude of fever, the purple cheek of pneumonia, the bright flush of phthisis, the contracted features and corrugated brow of tetanus—all these shades of countenance, and very many more which I might enumerate, with all their varieties of combination, are distinctly recognized by the experienced eye.[13]

Bright's associates at Guy's Hospital were, all of them, men of strong and striking personality. At this period Sir Charles Bell and Sir Benjamin Brodie, Travers, Liston and Pridgin Teale, were prominent figures, but Hodgkin and Addison were hardly ever heard of, and Bright, although he became in time the leading consultant in London, was little known outside of Guy's.[14] Ashton Key, another brilliant and able surgeon of Guy's, imposing in manner, but autocratic and quick-tempered, stalked through the wards, always wearing shepherd's plaid trousers, extending a forefinger for his dressers to shake.

Addison, a man of commanding appearance and imperious temper, was probably the ablest clinical lecturer of his time. He is described by Wilks and Bettany as

erect, with coat buttoned up very high, over which hung his guard and eyeglass. He wore a black stock with scarcely visible shirt collar, and this further elevated his head. He had a well-proportioned, good head, with dark hair and side whiskers, large bushy eyebrows and smallish dark eyes, nose thick, as were also the lips which enclosed his firmly knit mouth. His features were not refined, but belonged to a powerful mind, and showed no trace of any kind of sentiment. His penetrating glance seemed to look through you, and his whole demeanour was that of a leader of men, enhanced by his somewhat martial attitude. It is not surprising that the students worshiped him, and feared him rather than loved him; in fact, many thought him unapproachable, and never became closely attached to him. Many a student felt aggrieved, when bidding farewell to his master, that he failed in reciprocating the pupil's painful feeling of separation.

Yet Addison's manner, at times cold, haughty, blunt or even rude, was, he himself declared, only a cloak for nervousness. "It was only to some of his nearest friends that he disclosed some of the secrets of his life, his awful fits of despondency associated with some fearful circumstances which made him wonder that he was still alive to tell the tale." Wilks gives several anecdotes of his generosity and kindness of heart, and relates that he once checked a disparaging statement about an eminent physician with whom he had severed relations, by saying abruptly, "He is my colleague." Addison was, like Skoda, a diagnostician of extraordinary ability, but he attached so little importance to treatment that he sometimes forgot to prescribe. He died June 29, 1860.

Hodgkin, a member of the Society of Friends, always wearing their characteristic dress, was intended by nature for a philanthropist and social reformer and had the touch of eccentricity which often goes with that type of character. "On one occasion," it is related, "after sitting up all night with a man of very large fortune, Dr. Hodgkin offended him by filling up a blank cheque with the sum of £10, and made the offense still greater by telling him that 'he did not look as if he could afford more.' Dr. Hodgkin was never again sent for by the gentleman. It was difficult to make Dr. Hodgkin take the fees he had earned, and for this reason alone many of his friends would not consult him." Hodgkin left Guy's in 1837, having incurred the strong dislike of the autocratic treasurer, "King" Harrison, who, says Wilks, "would have no officer of the hospital who drove about with a North American Indian." He eventually dropped out of practice and devoted the rest of his life to the cause of persecuted Hebrews, emancipation, and similar philanthropies. He died at Jaffa, April 5, 1866, while travelling in the East with Sir Moses Montefiore, who erected the monument over his grave.

Of the three, Bright, who died December 16, 1858, was by far the best-balanced, a solidly built man of medium height, with a fine Thackerayesque head, a man of remarkably firm, even, self-contained character, and of cheerful, generous and unprejudiced disposition. Yet, in the days of Wakley's antagonism to Guy's even Bright did not escape the following, in which we recognize the familiar, testy ring of professional jealousy: "Bright and Addison give medicine; but Dr. Williams of St. Thomas's is far superior; for Bright is a heavy, conceited person and Addison a blustering bundle of loquacity. He will lecture for an hour on the causes of catarrh, and the distinction between lepra and psoriasis." In similar

[13] The minor discoveries of Bright afford most interesting correlations with modern work, but he himself, so rich in knowledge and so generous towards his colleagues, would have attached the least importance to priority. In the case of those original contributions of lesser men which have become buried by the dust of time, the question of priority is of capital importance, and some of the best historical research in recent times has been employed in bringing their work into prominence again. Sir William Osler rescued the obscure name of Hezekiah Beardsley from oblivion, and, as Dr. H. A. Kelly has shown, as far back as 1759, Mestivier, a forgotten French surgeon, performed an operation for appendicitis, the subsequent findings showing that not the cæcum, but the appendix alone was inflamed, the cause being a rusty pin inside the latter. As Dr. Billings said of the pioneer American surgeons in the backwoods "*les petits prophets*, as Verneuil styles them, are worthy of all honor," and one of the objects of the history of medicine is "to keep their names at least from being forgotten."

[14] I am indebted for these facts to Dr. Robert Fletcher, of Washington, D. C., who, about the time of Bright's retirement from practice, was a student at the London Hospital, and is, in fact, its oldest living graduate.

strain, Addison is elsewhere described as "a fine, dashing, big, burly, bustling man, proud and pompous as a parish beadle in his robes of office. Dark, and of a sallow complexion, an intelligent countenance and a noble forehead, he is what the ladies would pronounce a fine man. He has mentally and physically a tall idea of himself." Addison, in the light of what has been said, needs no defense, but the phrase "a heavy, conceited person" has been sometimes cited as a sort of half-truth in connection with the name of Bright. Of the character of the man who did so much to make internal medicine worthy of being called a "science," there can be no doubt. All his contemporaries agree that truth and honor, generosity and fair play were the essence of Bright's nature, and in the record of his travels, as in the story of his life, we do not find a trace of that over-estimation of self which we call self-conceit, the hallmark of intellectual dishonesty. His character reminds us of the truth of Emerson's aphorism that "Great men do not work for show." He was, as Wilks tells us, somewhat oblivious of the importance of his own work and incapable of anxiety about its future fortunes. But that this trait was far removed from priggishness is plain when we glance over his writings and see how he constantly delights in referring to the work of his colleagues, however obscure. In spirit he was no less than the "high-minded man" of the Nichomachean Ethics, but, at heart and in his private feelings, the old-fashioned Christian gentleman. His scientific work, like Addison's, reaches far out into the medicine of the future; and in the hundreds of pathological reports which he has so carefully recorded, it is probable that the physicians of to-morrow will find correlations as yet unthought of, an impression which the Reminiscences of Sir Samuel Wilks have amply and happily confirmed for the present time.

AUSTIN FLINT: HIS CONTRIBUTIONS TO THE ART OF PHYSICAL DIAGNOSIS AND THE STUDY OF TUBERCULOSIS.

By H. R. M. Landis, M. D., Philadelphia.

For those who take an interest in the achievements of American medicine, it cannot but be a source of pride that, of the small group of men who rounded out the work of Laennec, no apologies are needed when the name of Austin Flint is linked with that of Skoda, of Stokes and of Walshe.

We must not lose sight of the fact that Laennec's method, except by a few, was slow in being generally adopted. As late as 1856, Flint remarked, in the preface of his work on "Physical Exploration," that the method was employed by but a few physicians; many failed to practice it at all and not a few disbelieved in it altogether. Each country had its pioneer, and in this capacity if no other, American medicine owes much to Austin Flint.

Austin Flint was born in Petersham, Mass., October 20, 1812, four years before Laennec chanced on the discovery of mediate auscultation. This epoch-making discovery made possible modern clinical medicine, which was just emerging from its swaddling clothes when Flint began the study of medicine in 1832. It has been well said that the direction in which education starts a man will determine his future life; and of no man is this more true than of Austin Flint. He took up the study of medicine with a strong hereditary bias in its favor, his father, his grandfather and his great-grandfather having been physicians before him. Furthermore, fortune favored him in his choice of a school, for among his teachers were two remarkable men, Jacob Bigelow and James Jackson, who exerted a powerful influence on his life. His veneration for Laennec and his work unquestionably began in his student days, a brief glimpse of which he has left us.

"As early as 1832," he wrote, "when I attended medical lectures in Boston, James Jackson, the Professor of Medicine, then about to retire from medical teaching, was earnestly engaged in the subject of physical exploration. He never failed to carry the stethoscope during his hospital visits, and the signs of cardiac and pulmonary diseases entered largely into his clinical instructions."

Unlike many of his contemporaries, Austin Flint did not have the advantage of a European training. But so far from regretting it, he at one time advised young men against going abroad, expressing the belief that persisting industry and self-reliance would accomplish the desired results in this country. It must be confessed, however, that several of his objections were not convincing, namely, the temptations to pleasure and vice, which were to be met on every side, and the difficulty of acquiring the French tongue.

In the little more that half a century which elapsed between his graduation from the Harvard Medical School in 1833 and his death in New York on March 13, 1886, he enjoyed a peripatetic existence unusual even at a time when men not infrequently shifted from place to place. During this time, he practiced his profession or lectured in medical schools in no less than six widely separated localities.

A graphic description of the experience gained in these years has been written by his son. During his professional life he encountered "soldiers in camp and in barracks; the rich and the poor; those affected with diseases incident to lives of ease and luxury and paupers in hospitals; the pioneers of western New York and the inhabitants of the metropolis; patients in the wards of the Alms House and hospitals of Buffalo, of the Marine Hospital in Louisville, Ky., the great Charity Hospital in New Orleans, La., the Bellevue Hospital, the Charity Hos-

* Paper read at a meeting of The Laennec, A Society for the Study of Tuberculosis, The Johns Hopkins Hospital, February 26, 1912.

pital, the dispensaries and similar institutions in the City of New York; cases observed in the experience of a quarter of a century as a general practitioner, and of more than another quarter of a century as a consulting physician, including epidemics which have occurred in this country within the last fifty years." The records of these experiences, begun in 1833 and continued for more than half a century, covered sixteen thousand nine hundred and twenty-two folio pages of manuscript written with the author's own hand.

Shortly after his death, one of his most distinguished contemporaries, J. M. Da Costa, said of him: "With, perhaps, the single exception of Rush, there is no man who, in his many-sided capacities of teacher, author and investigator, has had thus far as much influence on the medicine of this country as Austin Flint." The number of students and practitioners whom he reached by his oral teachings and writings was enormous and unquestionably had much to do with the ultimate adoption of methods of physical exploration.

While a prolific writer on all phases of internal medicine, his reputation has endured largely because of his contributions to our knowledge of physical diagnosis and diseases of the heart and lungs. In this field he was preeminent, and most of his observations on the art of physical diagnosis are still authoritative.

A striking feature of his writings on physical diagnosis was the absence of theoretical speculation on the causation of signs. "The significance of signs which represent abnormal physical conditions," he observed, "rests on the uniformity of their association with the latter . . . . certain physical signs denote certain abnormal conditions, because clinical experience, inclusive of the study of lesions with the scalpel, has sufficiently established the fact."

Neither Laennec nor any of those who immediately followed him paid any attention to changes in the pitch of the percussion note or respiratory sounds. The value of pitch is now universally acknowledged and the credit for this addition to the art of physical diagnosis belongs to Austin Flint. His observations were embodied in an essay entitled, "Variations of Pitch in Percussion and Respiratory Sounds, and Their Application to Physical Diagnosis." This essay was awarded the annual prize of the American Medical Association in 1852. Our admiration for this essay cannot but be increased when we recall that the observations it records were those of one engaged in a country practice in Buffalo, then far distant from the large medical centers and little more than a frontier town.

The pathological significance of variations in the pitch of resonance, he says, may be stated in the following law: "An elevation of pitch always accompanies diminution of resonance in consequence of pulmonary consolidation. In other words, dulness of resonance is never present without the pitch being raised.

"The practical advantages to be derived from attention to pitch in employing percussion are that it confirms the existence of dulness and furnishes positiveness to the conclusion when the mere diminution of resonance might not be with certainty determinable; that it is of advantage, in some instances, when a disparity in the amount of resonance is inappreciable; and finally, it aids in developing a disparity in situations (supra- and infraspinous regions) in which but little resonance can be elicited owing to the intervention of bone, muscle and fat between the integument and walls of the chest."

In common with other observers of his time, he was familiar with the disparity of the percussion note in the infraclavicular regions, which he ascribed principally to an elevation of pitch on the right side. In one of his later contributions he described the percussion note in the right infraclavicular region as being vesiculo-tympanitic, emphasizing the fact that it was not dull but simply relatively less intense than on the left side. It is a remarkable testimony to his acuteness of sound perception that his analysis of the note produced in this situation has recently been satisfactorily explained by Drs. Norris and Fetterolf in a paper on differences in the percussion note over the two apices, read before the College of Physicians of Philadelphia. These observers have shown that the right apex is smaller than the left, being cone-shaped, while the left apex is dome-shaped; furthermore, the close proximity of the right apex to the trachea accounts for the tympanitic quality.

The great practical importance of elevation of pitch of the percussion note was, in his opinion, the aid it furnished in recognizing incipient tuberculosis when the deposit of tubercles was small in amount. "Any addition," he wrote, "to our means of giving precision to the diagnosis of incipient phthisis is a valuable consideration, not only to our science, but to our art, inasmuch as the prospect of saving or prolonging life is greater in proportion as the affection is earlier recognized."

A distinct advance also was made in our knowledge of the respiratory sounds by his study of changes of pitch. Bronchial breathing he pointed out was high in pitch, expiration being even higher than inspiration. Vesicular respiration, on the other hand, exhibits some striking points of dissimilarity. The inspiratory sound is lower in pitch, and the expiratory sound, when heard, save in a limited situation, is lower than the sound of inspiration.

Prior to his studies on pitch there was little or no attempt to differentiate cavernous from bronchial or tubular respiration. Flint pointed out that cavernous breathing was the exact opposite to bronchial respiration in that the inspiratory sound is low in pitch, non-vesicular in quality—a simple blowing sound—and the expiratory sound is still lower in pitch with the same quality.

Vesicular breathing, which is so frequently described as "breezy," "rustling," etc., never met with his approval. In his work on "Physical Exploration of the Lungs," published in 1856, he submitted the following inquiry:

"May not the peculiar quality be owing to the separation of the sides of the cells and the capillary tubes, which to a greater or less extent come into contact and, owing to the moisture of the tissues, are adherent during the collapse of the lung incident to expiration?" This conception evidently came from the explanation of the mechanism of the crepitant râle, given by Dr. E. A. Carr, of Canandaigua, N. Y., in 1842.

At another time he wrote, "It is noteworthy that Laennec,

in describing the differences between the vesicular murmur and bronchial respiration, says that the latter loses the 'slight crepitation' which belongs to the former. The expression 'slight crepitation' distinguishes more accurately than any other term the peculiar quality of the vesicular murmur, and, at the same time, it denotes the mechanism."

The term broncho-vesicular breathing, one of the most frequently used, and I might add, least understood, terms in physical diagnosis, was first described by Flint in 1852 under the name *rude* respiration. The term was introduced to embrace the abnormal variations between normal vesicular and bronchial respiration, the character of both being combined in variable proportions corresponding to the amount and extent of solidification. If the inspiratory sound has any recognizable vesicular quality, it is not bronchial but broncho-vesicular.

His description was as follows: "To form a correct idea of the modification usually termed *rude,* etc., it must be analytically decomposed, and the nature of its elements determined. It is an approximation to the bronchial respiration. It exhibits an incipient development of the character distinguishing the bronchial from the vesicular respiration. One of the most striking of these characters is the change in pitch. The pitch is raised. The vesicular quality is diminished; hence it approaches to a tubular or blowing respiration. The inspiration may be somewhat shortened and occasionally a sound of expiration becomes developed and prolonged, constituting an important rhythmical variation."

His final word on this type of respiration is as follows: "A case of pneumonia during the stage of resolution affords illustrations of all the gradations of this sign. The sign is present as soon as absorption has removed the contents of a sufficient number of air vesicles for a vesicular quality to be perceived in the sound of inspiration. The tubular quality now predominates, and the respiratory sound is still prolonged, high and tubular. With each successive day, as absorption progresses, the vesicular quality in the inspiratory sound increases, and the tubular quality diminishes. With these changes in the inspiratory sound, the expiratory sound on each successive day is less prolonged, less intense, less high in pitch and less tubular in quality. At length, resolution being complete, the vesicular quality becomes, for a time, more marked than in health, all the characters of the broncho-vesicular respiration having disappeared."

Just as under normal conditions there is a disparity in the percussion note in the infraclavicular region, so, too, does the character of the breath sounds differ, that at the summit of the right lung being broncho-vesicular in character. "Without a knowledge of these facts," he says, "it can hardly be otherwise than that an error of diagnosis will be committed, by mistaking for the physical signs of disease, the several characters of the bronchial respiration, which may exist at the summit of the right chest, not proceeding from a morbid condition. I am free to state that my own experience would supply illustrations of error from this source." Later, in 1881, in a paper on "An Analytical Study of Auscultation and Percussion," read before the International Medical Congress, he emphasized the fact that "a prolonged expiration is not a sign of phthisis unless the pitch be raised, and the quality more or less tubular."

His studies of pitch brought out changes also regarding the whispered voice. Laennec believed pectoriloquy almost pathognomonic of a cavity, and Walshe, who introduced whispering pectoriloquy, attached the same significance to this modification. Flint, however, showed that the whispered voice was also subject to variation of pitch, and that considerable diagnostic significance could be attached to these variations. Thus, in differentiating between consolidation and an excavation, the whispered voice in the former is high in pitch, tubular, and resembles bronchophony; in the latter it is low in pitch and blowing. "The differential characters thus, as is evident must be the case, correspond to those of expiration in the cavernous and the bronchial respiration," as the whisper is usually an act of expiration.

To Austin Flint must be credited the practical application of the fact that fluid in the chest cavities changes its level with alterations of the position of the patient. His observation on movable dulness in cases of pleural effusion is as follows: "Without taking pains to demonstrate the variation of the level too elaborately, which is not always convenient in practice, if the upper limit of the flatness in front be ascertained by percussion, while the trunk is in a vertical position, then cause the patient to lie down, and ascertain if the resonance does not extend an inch or more below the point at which, in the previous position, the upper limit of flatness was found to exist." (Physical Exploration of the Lungs, 1856.)

He also called attention to the fact that in cases of perforation of the stomach or intestines, liver dulness was obliterated or greatly diminished.

While he was an equally close student of the physical signs related to the heart, he did not add much of an original nature to this aspect of physical diagnosis. In 1858, he submitted an essay on variations of pitch of the heart sounds, which like its predecessor on "Variations of Pitch in Percussion and Auscultation" received the annual prize offered by the American Medical Association.

Curiously enough, his name is most frequently recalled today by reason of its being associated with the presystolic murmur which sometimes accompanies aortic regurgitation. The association of a physical sign with the name of its describer was a practice he did not approve of. "So long," he wrote, "as signs are determined from fancied analogies, and named from these or after the person who describes them, there cannot but be obscurity and confusion."

The first time he observed the so-called "Flint murmur" was in 1859, in a patient in the Charity Hospital in New Orleans, who had well-marked signs of double aortic disease and a presystolic murmur at the apex. At the autopsy, however, the mitral valves were found to be normal. The cause of this phenomenon, given in 1862 (American Journal Medical Sciences), is as follows: "The explanation involves a point connected with the physiological action of the auricular valves. Experiments show that when the ventricles are filled with a liquid, the valvular curtains are floated away from the ventricular sides,

approximating to each other and tending to closure of the auricular orifice. . . . Now in cases of considerable aortic insufficiency the left ventricle is rapidly filled with blood flowing back from the aorta, as well as from the auricle, before the auricular contraction takes place.

"The distention of the ventricle is such that the mitral curtains are brought into coaptation, and when the auricular contraction takes place the mitral direct current, passing between the curtains, throws them into vibration and gives rise to the characteristic blubbering murmur. The physical condition is in effect analogous to contraction of the mitral orifice from an adhesion of the curtains at their sides, the latter condition, as clinical observation abundantly proves, giving rise to a mitral direct murmur of a similar character."

His contributions to the study of tuberculosis are among the best, from a clinical standpoint, which our literature contains, and if he can be said to have had any special preference, it was for the study of this disease. From his earliest contribution on the subject, in 1849, he continued to be a close student of tuberculosis in all its phases, and while ever ready to accept new advances as to its etiology, he resisted strongly the various theories advanced to disprove its unity. Especially worthy of mention is the monograph on "Phthisis" published in 1875. This is a masterly analysis of over six hundred and seventy cases, and deserves to be ranked with the great work of Louis, after which, indeed, it was modeled.

Dr. Edward L. Trudeau has sketched for us the attitude of the medical profession towards tuberculosis in 1873, in the following words: "The climatic treatment was within the reach of only a small class of patients, namely, the well-to-do; and they were not generally sent away until their physician, or they themselves, became alarmed at the activity of their symptoms. The poor, and the large class of men and women who depended upon their daily work for their support, were left to their fate. No special stress was laid on the early recognition of the disease, as it was generally believed to be fatal. This, then, was approximately the attitude of the profession and the public towards tuberculosis when I went to the Adirondacks in 1873."

Probably the greatest service Austin Flint rendered to the study of tuberculosis was his insistence on the importance of recognizing the disease in its incipiency. From his earliest article on the subject in 1849, he constantly emphasized this point as being "immensely important by the fact that the prospect of exerting a control over the disease and diminishing its tendency to a fatal issue, is in proportion to its early recognition." In the essay on "Variations of Pitch, etc.," published in 1852, the most important practical deductions he made were with reference to this point.

The following cases, taken from the essay on pitch, are illustrative of what he considered incipient tuberculosis:

(1) Cough for two months and slight expectoration. Slight dulness in right infraclavicular region. Expiration prolonged and similar in pitch to inspiration with an interval between inspiration and expiration. This case was doubtful but afterwards was conclusively shown to be tuberculous.

(2) Cough, slight expectoration. Chest pain and an occasional night sweat. Slight dulness in left infraclavicular region, also posteriorly over scapula; bronchophony; pitch of respiration is in a marked degree higher on the left than the right, at the summit of the chest anteriorly and posteriorly. The elevation in pitch is the chief disparity between the two sides.

Of course, more recent studies of the breath changes in early tuberculosis have enabled us to anticipate even the stage depicted by Flint, but the fact remains that the majority of cases of early tuberculosis to-day are recognized by the signs he emphasized sixty years ago.

He was thoroughly alive to the importance of certain symptoms which mark the onset of tuberculosis, such as hemoptysis and a persistent cough. Of the former, he wrote:

"Hemoptysis occurs in some cases when not only the symptoms of pulmonary disease are wanting, but the result of physical explorations of the chest is negative." "Prudence dictates that, in the cases in which hemoptysis is the only evidence of pulmonary disease, it is wise to act as if phthisis either exists or is impending."

And again, "Another conclusion is, that hemoptysis is not a cause of phthisis, as was asserted by Niemeyer. This is a fair inference from the fact that in only about one-third of the cases in which hemoptysis occurred as an antecedent event, was it immediately followed by the evidence of pulmonary disease, an interval of weeks, months or years elapsing in two-thirds of the cases."

Of cough, he said, "I do not claim, in behalf of this symptom, that it always denotes the precise time when phthisis begins. That, as a rule or often, a persistent cough precedes the development of phthisis, I do not believe. It seems to me fair to conclude that the disease existed when such a cough began; but it is not so clear that a cough always attends the beginning of phthisis."

In view of the acrimonious discussions that have raged for years regarding the value of this or that climate, the following, written in 1875, is of interest:

"My studies seem to lead to conclusions at variance with the prevailing popular and professional belief in a special climatic influence. In the first place, it does not appear from the analysis of my cases that changes of climate have in a marked degree a beneficial influence, as compared with the hygienic measures available at home. In the second place, the improvement following a change appears to pertain alike to different climates and places. Hence, it seems a fair inference that the benefit derived from the change is due, not so much to a climatic influence, *per se*, as to the circumstances incidental to the change. These circumstances are often a change of habits from those which are sedentary and confining within doors, to those involving out-of-door life and activity, freedom from the cares, anxieties and annoyances of business at home, and, it may be added, the moral effect of the hope or expectation of being benefited by climatic influences."

His study of the natural history of disease led him to a belief that phthisis was to a certain extent self-limited and that recovery frequently occurred whether anything was done or not.

and in some instances in spite of what was done. In an analysis of seventy-five cases ending either in complete recovery or non-progression of the disease, he showed that in one-half of them there had been no treatment whatever which could be said to have brought about the favorable result.

Of another important phase of the treatment of tuberculosis he wrote: "The importance of alimentation in this disease may be measured by the significance in prognosis of appetite, digestion and nutrition. Recovery cannot take place, the disease, in fatal cases, will not be very slowly progressive, its duration prolonged, tolerance of it maintained, if the conditions of assimilation do not approximate to those of health. This statement is sustained alike by clinical experience and common sense. Hence, alimentation is an essential part of the treatment."

One of the distinguishing features of Austin Flint was the receptivity of his mind. He was ever ready to discard the old and accept the new, providing the latter bore the evidences of truth. The reproach of opposing a new advance because it was contrary to accepted belief cannot, in a single instance, be brought against him.

Shortly after Koch's paper on the etiology of tuberculosis appeared, he began having the sputum of the patients at the Bellevue Hospital examined and quickly assured himself of the importance of the discovery. In a paper read a short time afterwards (he was then in his seventy-second year), he pointed out that it was a rational supposition that the danger of contracting phthisis was probably proportionate to the degree of exposure to the contagion. "In short," he remarked, "I have applied to pulmonary phthisis well-known truths as applied to other infectious diseases. These truths are novel, and may seem startling in their application to pulmonary phthisis, because, up to the present time, few physicians have been accustomed to look upon this disease as belonging to the infectious diseases."

The extraordinary elasticity of his mind enabled him even to peer into the future. There has been scarcely an advancement made since his death that would cause him any great surprise or wonder, for that most of them would happen, he predicted in the last article he ever wrote, which was published after his death. In "Medicine of the Future" he foresaw that chemistry, both physiological and pathological, must be sought for to explain many of the phenomena of health and disease. The rôle of bacteria he had already accepted and clearly foresaw the advance in this branch. "I assume it to be a demonstrated truth," he wrote, "that the specific causes of certain of the infectious diseases are micro-organisms. If my reasoning be correct, it is simply a question of time as to the discovery of specific organisms for all the infectious diseases." The recording of the movements of the heart by the electro-cardiogram, when the instrument is at a great distance from the patient and even in another building, he would have accepted as a matter of course, for he wrote regarding the telephone and telegraph, "I will go further and say that the intrathoracic sounds may be transmitted from the patient to the physician, no matter how distant may be the one from the other."

Inasmuch as I already have quoted so liberally from his writings, I can do no better than apply to him his own estimate of Laennec:

"The career of the distinguished man, whose biography has been our theme on this occasion, is preeminently worthy of admiration. In his character were beautifully blended the finest intellectual and moral qualities of our nature. With mental powers of the highest order, were combined simplicity, modesty and purity and disinterestedness, in such measure that we feel he was a man to be loved not less than admired."

CYRANO DE BERGERAC'S OPINION OF THE MEDICAL PROFESSION.

By Charles Greene Cumston, M. D., Boston, Mass.

It is evident, from his letter entitled *Contre les Médecins,* that Cyrano de Bergerac was ill-disposed towards the medical profession. Such feeling was not new in his day, because the predecessors of the immortal Molière, during the period from 1650, *Le Médecin Volant,* to 1673, *Le Malade Imaginaire,* were dealing terrible blows at the "learned body" and, with Cyrano, endeavored to destroy the Gothic prejudices, and fought against the ancient blind and obstinate schools which were opposed to the progress of science.

The physicians cast discredit upon themselves by calling each other impostors and charlatans. Scarron, Barclay, La Fontaine, Boileau, La Bruyère continued the struggle against the profession; so did the author of *Valesiana.* "Can it be that one questions what great national and social interest there may be in having placed physicians and medicine in this pillory of satire, after having witnessed the insanity, both grostesque and criminal, of the doctrines and practice then in vogue? Can it be that one does not detect the inspiration of a sentiment of humanity and the accomplishment of a patriotic duty in this enterprise of public salubrity by ridicule?" In Cyrano's letter *Contre les Médecins* the intent is not only the act of a man who runs down a half-vanquished enemy, but a courageous attack of a libertine who makes himself the auxiliary of common sense. He was condemned and "just as criminals preach to the people from the gallows," he wished to speak to the youth of his day. *Et nunc erudimini!* He fell into the hands of *Dr. Tant Mieux,* and "from being in good health, he dies . . . Admire the effrontery of my executioner; the more I feel the disease increasing which he causes by his medicines, and the more I complain of some new symptom, the more he evinces his joy and dresses my wounds with nothing more than a '*Tant mieux.*' When I tell him that I had fallen into a lethargic syncope which lasted for an hour, he replies that it is a good sign. When he sees me in the clutches of a flux of

blood which tears me asunder: 'Good,' says he, 'that is equal to a bleeding!' When I complain of feeling like an icicle which involves all my limbs, he laughs, assuring me that he well knew that his remedies would extinguish this great fire. Sometimes even when, like Death, I cannot speak, I hear him say to those about me who are in tears on account of my serious condition: "Poor fools that you are, do you not perceive that it is the fever which is near its close?" What a fine art is medicine and how simple to practice! "What honors and riches it brings to those who cultivate it!" If the patient escapes, "the recovery is attributed to potent remedies"; and "if he dies, everyone says that he (the physician) is a clever man and had said it would occur."

Consequently, according to Cyrano we should all become physicians "so as to put under the earth those who have placed us there." A horrible and fatal profession, and to dream that one has met one of it "is capable of producing fever." "Whether it is a tertian or quartan," these clever fencers deliver us to the clergy, who chant over our cadavers. And he ends his satire by chasing away his "graduated Demon." *Vade retro, Satanas,* that is to say, remember that the reform undertaken by Bacon in the sciences, each year gains ground, that Descartes has dethroned Aristotle and that he can say of science: *Nos descendants grossiront ce dépôt qui doit s'augmenter d'âge en âge!* . . . and to those dangerous ignorants will succeed the marvelous savers of the poor human race.

I will now transcribe the letter *in extenso,* as it is little known to medical historians and, as a document, cannot be devoid of interest.

Monsieur,

Puisque je suis condamné (mais ce n'est que du Médecin, dont j'apellerai plus aisément que d'un arrêt prévôtal), vous voulez bien que, de même que des criminels qui prêchent le peuple quand ils sont sur l'échelle, moi qui suis entre les mains du Bourreau, je fasse aussi des remonstrances à la jeunesse. La Fièvre et la Drogueur me tiennent le poignard sur la gorge avec tant de rigueur, que j'espère d'eux qu'ils ne souffriront pas que mon discours vous puisse ennuyer. Il ne laisse pas, Monsieur le Gradué, de me dire que ce ne sera rien, et proteste cependant à tout le monde que, sans miracle, je n'en puis relever. Leurs présages, toutefois, encore que funestes, ne m'alarment guère; car je connois assez que la souplesse de leur art les oblige de condamner tous leurs malades à la mort, afin que, si quelqu'un en échappe, on attribue la guérison aux puissans remèdes qu'ils ont; et, s'il meurt, chacun s'écrie que c'est un habil homme et qu'il avoit bien dit. Mais admirez l'effronterie de mon Bourreau: plus je sens empirer le mal qu'il me cause par ses remèdes, et plus je me plains d'un nouvel accident, plus il témoigne s'en réjouir et ne me panse d'autre chose que d'un *Tant Mieux!* Quand je lui raconte que je suis tombé dans un syncope léthargique qui m'a duré près d'une heure, il répond que c'est bon signe. Quand il me voit entre les ongles d'un flux de sang qui me déchire: "Bon!" dit-il, "cela vaudra une saignée!" Quand je m'attriste de sentir comme un glaçon qui me gagne toutes les extrémités, il rit, en m'assurant qu'il le savoit bien, que ses remèdes éteindroient ce grand feu. Quelquefois même que, semblable à la Mort, je ne puis parler, je l'entends s'écrier aux miens qui pleurent de me voir à l'extrémité: "Pauvres nigauds que vous êtes, ne voyez-vous pas que c'est la fièvre qui tire aux abois?" Voila comme ce traitre me berce; et cependant, à force de me bien porter, je me meurs. Je n'ignore pas que j'ai grand tort d'avoir réclamé mes ennemis à mon secours. Mais quoi? pouvois-je deviner que ceux dont la science fait profession de guérir l'emploieroient tout entière à me tuer? car, helas! c'est ici la première fois que je suis tombé dans la fosse; et vous le devez croire, puisque si j'y avois passé quelque autre fois, je ne serois plus en état de m'en plaindre. Pour moi, je conseille aux foibles Lutteurs, afin de se venger de ceux qui les ont renversés, de se faire Médecins, car je les assure qu'ils mettront en terre ceux qui les y avoient mis. En vérité, je pense que de songer seulement, quand on dort, qu'on rencontre un Médecin, c'est capable de donner la fièvre. A voir leurs animaux étiques, affublés d'un long drap mortuaire, soutenir immobilement leur immobile maître, ne semble-t-il pas q'une bière ou la Parque c'est mise à califourchon, et ne peut-on pas prendre leur houssine pour le guidon de la Mort, puisqu'elle sert à conduire son Lieutenant? C'est pour cela sans doute que la Police leur a condamné de monter sur des mules et non pas sur des cavales, de peur que la race des gradués venant à croître, il n'y eût à la fin plus de bourreaux que de patiens. Oh! quel contentement j'aurois d'anatomiser leurs mules, ces pauvres mules qui n'ont jamais senti d'aiguillon, ni dedans, ni dessus la chaire, parce que les éperons et les bottes sont des superfluités que l'esprit délicat de la Faculté ne sauroit digérer! Ces Messieurs se gouvernent avec tant de scruple, qu'ils font même observer à ces pauvres bêtes (parce qu'elles sont leurs domestiques) des jeûnes plus rigoureux que ceux des Ninivites, et quantité de très-longs, dont le Rituel ne s'etoit point souvenu: ils leur attachent, par les diètes, la peau tout à cru dessus les os, et ne nous traitent pas mieux, nous qui les payons bien; car ces Docteurs morfondus, ces Médecins de neige, ne nous font manger que de la galée. Enfin, tous leurs discours sont si froids, que je ne trouve qu'une différence entre eux et les peuples du Nord, c'est que les Norwégiens ont toujours les mules. Ils sont tellement ennemis de la chaleur, qu'ils n'ont pas sitôt connu dans un malade quelque chose de tiède, que, comme si ce corps étoit un Mont-Gibel,* les voila tous occupés à saigner, à clistériser, à noyer ce pauvre estomac dans le séné, la casse, la tisane, et à débiliter la vie pour débiliter, disent-ils, ce feu qui prend nourriture, tant qu'il rencontre de la matière; de sorte que, si la main tout expresse de Dieu les fait rejamber vers le monde, ils l'attribuent aussitôt à la vertue de réfrigératifs dont ils ont assoupi cet incendie. Ils nous dérobent la chaleur et l'énergie de l'être qui est au sang: ainsi, pour avoir été trop saignés, nos Ames, en s'envolant, servent de volant aux palettes de leurs chirurgiens. Eh bien, Monsieur, que vous en semble? Après cela, n'avons-nous pas grand tort de nous plaindre de ce qu'ils demandent dix pistoles pour une maladie de huit jours? N'est-ce-pas une cure à bon marché où il n'y a point de charge d'âmes? Mais confrontez un peu, je vous prie, la ressemblance qu'il y a entre le procédé des Drogueurs et le procédé d'un Criminel. Le Médecin, ayant considéré les urines, interoge le patient sur la selle, le condamne; le Chirurgien le bande et l'Apothicaire décharge son coup par derrière. Les affligés même, qui pensent avoir besoin de leur chicane, n'en font pas grande estime. A peine sont-ils entrés dans la chambre, qu'on tire la langue au Médecin, on tourne le cul à l'Apothicaire et l'on tend le poing au Barbier. Il est vrai qu'ils s'en vengent de bonne sorte: il en coûte toujours au Railleur le cimetière. J'ai remarqué que tout ce qu'il y a de funeste aux Enfers est compris au nombre de trois: on y voit trois fleuves, trois chiens, trois juges, trois Parques, trois Gerions, trois Hécates, trois Gorgones, trois Furies. Les fléaux dont Dieu se sert à punir les hommes sont divisés aussi par trois: la peste, la guerre et la faim; le monde, la chair et le diable; la foudre, le tonnerre et l'éclair; la saignée, la médecine et le lavement. Enfin, trois sortes de gens sont envoyés au monde tout exprès pour martyriser

* Popular name for Etna.

l'homme pendant la vie: l'Avocat tourmente la bourse, le Médecin le corps, et le Théologien l'âme. Encore ils s'en vantent, nos Ecuyers à mules! car, comme un jour le mien entroit dans ma chambre, sans autre explication, je ne lui fis que dire: *Combien?* L'impudent meurtrier, qui comprit aussitôt que je lui demandois le nombre de ses homicides, empoignant sa grosse barbe, me répondit: "*Autant!* Je n'en fais point, continua-t-il, la petite bouche, et, pour vous montrer que nous apprenons aussi bien que nous nous exerçons, de même qu'eux, toute nôtre vie, sur la tierce et sur la quarte." La reflexion que je fis sur l'innocence effrontée de ce personnage fut que si les autres disoient moins, ils en font bien autant; que celui-là se contentoit de tuer, et que ses comerades joignoient au meutre la trahison; que, qui voudroit écrire les voyages d'un Médecin, on ne pourroit pas les compter par les épitaphes de sa Paroisse, et qu'enfin, si la fièvre nous attaque, le Médecin nous tue et le Prêtre en chante. Mais ce seroit peu à Madame la Faculté d'envoyer nos corps au sépulcre, si elle n'attentoit sur notre âme. Le Chirurgien enrageroit, plutôt qu'avec sa charpie tous les blessés qui font naufrage entre ses mains ne fussent trouvés morts couchés avec leurs tentes.* Concluons donc, Monsieur, que tantôt ils envoient et la Mort et sa faux ensevelies dans un grain de mandragore, tantôt liquifiée dans le canon d'une seringue, tantôt sur la pointe d'une lancette; que, tantôt, avec un juillet, ils nous font mourir en octobre, et qu'enfin ils sont accoutumés d'envelopper leurs venins dans de si beaux termes, que dernièrement je pensois que le mien m'eût obtenu du Roi une Abbaye commendataire, quand il m'assura qu'il m'alloit donner un Bénéfice de ventre. Oh! qu'alors j'eusse été réjoui si j'eusse pu trouver à le battre par équivoque, comme fit une Villageoise à qui un de ces Bateleurs demandant si elle avoit du pouls, elle lui répondit avec force soufflets et force égratignures, qu'il étoit un sot, et qu'en toute sa vie elle n'avoit jamais eu ni poux ni puces! Mais leurs crimes sont trop grands pour ne les punir qu'avec des équivoques; citons-les en justice de la part des Trépassés. Entre tous les humains, ils ne trouveront pas un Avocat; il n'y aura Juge qui n'en convainque quelqu'un d'avoir tué son père; et, parmi toutes les pratiques qu'ils ont couchées au cimetière, il n'y aura pas une tête qui ne leur grince les dents. Que les pussent-elles dévorer! Il ne faudriat pas craindre que les larmes qu'on jetteroit de leur perte fissent grossir les rivières: on ne pleure, aux trépas de ces gens-là, que de ce qu'ils ont trop vécu. Ils sont tellement aimés, qu'on trouve bon tout ce qui vient d'eux, même jusqu'à leur mort; comme s'ils etoient d'autres Messies, ils meurent aussi bien que Dieu pour le salut des hommes. Mais, bons Dieux! n'est-ce pas encore là mon mauvais Ange qui s'approche? Oh! c'est lui-même! je le connois à sa soutane. *Vade retro, Satanas!* Champagne, apportez-moi le bénitier. Démon gradué, je te renonce! Oh! l'effronté Satan! Ne me viens-tu pas encore donner quelque aposume? Misericorde! C'est un Diable huguenot, il ne se soucie point de l'eau bénite! Encore, si j'avois des poigns assez roides pour former un casse-museau; mais, hélas! ce qu'il m'a fait avaler c'est si bien tourné en ma substance, qu'à force d'user de consommés, je suis tout consommé moi-même. Venez donc vitement à mon secours, ou vous allez perdre,

Monsieur,

Votre plus fidèle Serviteur

D. C. D. B.

TRANSLATION.

[Sir,

Since I am condemned (but only so by the physician, from whom I can appeal more easily than from a prevotal judgment) you wish me, being in the hands of my executioner, to address the youth as criminals do the people when on the scaffold. Fever and the Drugger hold a dagger over my throat with such rigor, that I hope they will not permit my discourse to weary you. Monsieur the Graduate does not cease to tell me that it is nothing and never the less, protests to everyone, that unless some miracle occurs, I may never get up. However, their foreboding, although sombre, hardly alarmes me, for I know well that the cunning of their art forces them to condemn all their patients to death, so that should some escape, the cure will be attributed to the powerful remedies employed, and, if one dies, everyone says what a clever man he (the physician) was and how truly he had spoken. But please admire the impudence of my executioner; the more my affection increases by the use of his remedies, and the more I complain of some new symptom, the more he manifests his pleasure and only dresses my wounds with a "*So much the better!*" When I tell him that that I have had a lethargic syncope which lasted nearly an hour, he replies that it is a good sign. When he sees me in the clutches of a flux of blood which tears me to pieces: "Good, says he, that is equal to a bleeding." When I sadly tell him that I feel like an icicle which involves my limbs, he laughs, assuring me that he well knew it, that his remedies will extinguish this great fire. Sometimes even, when like Death, I cannot speak, I hear him tell those about me who weep for my serious condition: "Poor fools that you are, do you not see that it is the end of the fever?" Thus does this traitor treat me; and, never the less, in spite of being well, I kill myself. I am fully aware that I am wrong in having called my enemies to my aid. But now! could I have suspected that those who's science professes to cure, would employ it for killing me? because, alas! this is the first time that I have fallen into the ditch, and so you must think, because had I been there before, I should now be in no condition to complain. I advise all feeble strugglers, in order to avenge themselves upon those who have overturned them, to become physicians, because I can assure them that they can put under ground those that have put them there. In truth, I think that to even dream that one has met a physician, is quite enough to give one a fever. To see their lank animals, covered with a long mortuary cloths, motionlessly supporting their motionless master, would it not seem that a coffin or the Parcæ had straddled them, and not to mistake their switch for the guide to Death, since it serves to conduct its Lieutenant? It is for this reason, undoubtedly, that the Police have ordered them to ride on mules and not on horses, for fear that the race of graduates by increasing, there would at length be more executioners than patients. Oh! how happy would I be to dissect their mules, these poor mules who have never felt the spur, neither within nor over their flesh, because spurs and boots are superfluities that the delicate mind of the Faculty could never digest! These Gentlemen govern themselves with so great a scruple, that they even oblige these poor beasts (because they are their servants) to resort to fasts more rigorous than those of the Ninivites, which the Ritual had quite forgotten; by diet, they attach their skin to their bones, and do not treat us, who pay them well, any better; because these Doctors who strike a chill into one, these Physicians of snow, only allow us to eat frost. Then again, their discourse is so cold, that I find only one difference between them and the Northern people, and that is that the Norwegians always have chill-blains on the heels while they always have their heels on the mules. They are such enemies of heat, that just as soon as they have discovered something tepid in a patient, that, as if this body was an Etna, there they are bleeding, giving enemata, drowning this poor stomach in senna, cassia, diet drinks, and debilitating life in order to debilitate, say they, this fire which takes nourishment wherever there is matter (that is, food for it); so that, if the hand of God expressly makes them return to earth they at once attribute it to the virtue of their refrigerating drugs by which they have extinguished the conflagration. From us they remove the heat and

* A pun: *tente*, which is pronounced *tante*, is the name given to lint (charpie) used by surgeons in dressing wounds. It was inserted into the wound.

energy of the being which is in the blood and thus, for having been bled too much, our souls flit off, serving as shuttle-cocks to the pallets of their surgeons. Well, Sir, what do you think? After this, are we not very wrong to complain when they ask ten pistols for a disease which lasts eight days? Is not this a cheap cure where there is no charge of souls? But compare a little, I beg of you, the resemblance there is between the procedures of the Druggers and those of a Criminal. The Physician, having considered the urine, questions the patient as to his stools and condemns him; the Surgeon bandages him and the Apothecary discharges his shot in the back sides. Even the afflicted, who think they have need of their cavilling, hold them in small estimation. Hardly have they entered the room, than one sticks his tongue out at the Physician, the back sides are turned to the Apothecary and the fist is offered to the Barber. It is true that they thoroughly avenge themselves; the cemetary is the price paid by the Jester. I have noted that all that is fatal in Hell is comprised in the number three; there are there three rivers, three dogs, three judges, three Fates, three Gerions, three Hecates, three Gorgons, three Furies. The plagues which God employs to punish man are also divided by threes: The plague, war and hunger; the earth, the flesh and the devil; the thunderbolt, thunder and lightening; bleeing, purgatives and enemata. Lastly, three kinds of people are put upon earth expressly for martyrizing man during his life: The lawyer torments the pocket-book, the Physician the body and the Theologian the soul. And they brag about it, our mule-mounted Squires! because, one day when mine entered the room, without other explanation, I only said: "*How many?*" The impudent murderer, who understood at once that I asked him the number of his homicides, stroking his big beard, replied: "*So much!* I commit none," continued he, playing the difficult, "and to show you that we learn quite as well as Fencers, the art of killing, we like them, exercise our entire life on tertian and quartan fever." The reflexion that I made on the impudent innocence of this person was that if others said less they did quite as much; that this one contented himself with killing and that his comrades joined treason with murder; that he who would write the travels of a Physician could not count them by the number of epitaphs in his Parish, and that, lastly, if fever attacks us the Physician kills us and the Priest sings of it. But it would be little for Madame la Faculté to send our bodies to burial if she did not involve our souls. The Surgeon would be angry, rather than with his lint, all the wounded who are wrecked by his hands were not found dead and lying with their tents. Let us conclude, Sir, that, at times they send both Death and his scythe burried in a grain of mandrake, at others liquified in the barrel of a syringe, and still again at the point of the lancet; that sometimes with a July, they make us die in October, and that they are accustomed to surround their poisons in such fine terms that, laterly, I thought that my physician would have obtained for me a commendatory Abbey from the King, when he assured me that he was about to give me a privilege of the belly. Oh! then would I have rejoiced could I have but found the means to combat him by equivocation, as did the peasant woman to whom one of these jugglers asked if she had a pulse, when she replied by numerous blows and scratches that he was a fool and that in all her life she had never had either lice or flees! * But their crimes are too great to be punished only by equivocation; let us bring them to justice on behalf of the Dead. Among all the living they will not find a single Lawyer; there is not a Judge who will not convict some one of them of having killed his father; and among all the clients that they have placed in the grave yard, there is not a single skull which does not grind his teeth. Could they but devour them! It is not to be feared that the tears shed for them at their death would make large rivers: one only cries at their death because they lived too long. They are so beloved, that everything done by them, even their death, is good; as if they were other Messiahs, they die just as God did, for the salvation of men. But, great Gods! is not my bad Angel approaching again? Oh! t'is he himself! I know him by his cassock. *Vade retro, Satanus!* Champagne, bring me the holy-water basin. Graduate Demon, I renounce thee! Oh! impudent Satan! Comest thee again to give me another medicinal decoction? Misericorde! it is a huguenot Devil who cares nothing for holy water! Again, if I only had fists sufficiently strong for a break-snout; but, alas! what he made me swallow has so well turned within my substance, that from using consommés I am myself completely consumed. Come then, quickly to my rescue or you will lose

Sir,

Your most faithful Servant

D. C. D. B.]

* By comparing the French, one will see the play on the prononciation of *pouls* and *poux*.

Comment is quite unnecessary. Cyrano has set forth in the above lines the consensus of public opinion regarding the faculty of medicine of Paris. As an illustration of the narrow-mindedness of its members, it is enough to say that Harvey's discovery of the circulation was not admitted by that body until some twenty years later. The ancient authors were alone considered, and not until the caustic satire of Molière had wrought its good work, did the teachings of Hippocrates and Galen disappear and the great truths fast coming to light were accepted.

NOTES AND NEWS.

ARMY MEDICAL CORPS EXAMINATIONS.

The Surgeon General of the army announces that preliminary examinations for the appointment of first lieutenants in the army medical corps will be held on July 15, 1912, and September 3, 1912, at points to be hereafter designated.

Full information concerning these examinations can be procured upon application to the "Surgeon General, U. S. Army, Washington, D. C." The essential requirements to securing an appointment are that the applicant shall be a citizen of the United States, shall be between 22 and 30 years of age, a graduate of a medical school legally authorized to confer the degree of doctor of medicine, shall be of good moral character and habits, and shall have had at least one year's hospital training, after graduation. The examinations will be held concurrently throughout the country at points where boards can be convened. Due consideration will be given to localities from which applications are received, in order to lessen the traveling expenses of applicants as much as possible.

The examination in subjects of general education (mathematics, geography, history, general literature, and Latin) may be omitted in the case of applicants holding diplomas from reputable literary or scientific colleges, normal schools or high schools, or graduates of medical schools which require an entrance examination satisfactory to the faculty of the Army Medical School.

In order to perfect all necessary arrangements for the examination, applications must be complete and in possession of the Adjutant General at least three weeks before the date of examination. Early attention is therefore enjoined upon all intending applicants. There are at present sixty-eight vacancies in the medical corps of the army.

NOTES ON NEW BOOKS.

The Treatment of Fractures by Mobilisation and Massage. By James B. Mennell, M. D. With an introduction by Dr. J. Lucas-Championnière. $4.00. (*London: Macmillan & Co., Limited, St. Martin's Street, 1911.*)

The methods of treatment advanced in this book are founded very largely on those of Professor Lucas-Championnière of Paris. The author says that the pathology of the results obtained in the treatment of fractures by "massage and mobilisation" has not yet been completely worked out, so especial attention will be given to the practical results.

Careful notes on over 400 cases thus treated form the basis of the work. The book is divided into two parts. In Part I, the general subject of fractures is considered and the methods of procedure under this form of treatment. In Part II, the detail of the treatment of individual fractures is taken up.

The author treats all fractures by a painless, gentle massage, which is called "glucokinesis," "The movements of which are little more than a caress, being so smooth and light that they almost resemble a mesmeric pass." "Whatever the movement may be it is to be performed slowly, not more than ten or twelve times to the minute. It must be repeated with inexorable regularity, both as regards direction and rapidity. The direction should coincide with that of the venous flow or of the underlying muscular fibers." "The one criterion of the massage is that it should be painless. Moreover, if pain be present, the massage must relieve it; otherwise the technic is at fault."

About fifteen minutes each day is devoted to the massage. In addition to the massage, "mobilisation" by active and passive motions is necessary. "Four rules govern this portion of the treatment. The movements must be painless; amplitude of movement must be sacrificed to frequency; all movements possible of each point of the injured limb must be performed; and no joint in the injured limb must be neglected." Splints are used for a short time as an adjunct to the above treatment. "The use of splints for four days will prove sufficient for the majority of fractures, a week for the remainder, except possibly for fractures of the femur, where there has been great displacement with consequent tearing of the periosteum."

I will mention one case reported by the author to illustrate the above treatment: A patient with a "back fire" fracture through the lowest inch of the radius came in after a sleepless night suffering great pain. The radiograph showed a fracture into the joint, with great comminution and considerable spreading of the fragments. The forearm was much swollen as was the lower portion of the arm; there was much bruising and every joint below the elbow was perfectly rigid. After fifteen minutes massage all pain had disappeared and the patient could move the fingers and thumb almost freely; slight painless movements were performed at the wrist, and the elbow movements were completely restored. From this time there was no further pain. The splints were abandoned in five days and at the end of a week the patient was performing various exercises and using his hand for feeding, etc. In less than six weeks he was on full duty.

There are four possible contraindications to this method noted by the author. Excessive mobility of the fragments, skin lesions, extreme youth of the patient, and extreme old age. However, he says that none of these are absolute contraindications.

From the above very brief outline an idea of the method can be obtained. There are a number of valuable points brought out on the general subject of fractures, but it is difficult to accept some of the author's ideas.

There is no doubt but that most of us are disposed to keep a broken bone at rest in a fixation apparatus of one sort or another, for a longer time than is absolutely necessary, but the removal of such support as early as the author advises seems to one who has had no experience in treating fractures entirely by "mobilisation and massage" to be somewhat radical. The use of "massage and mobilisation" has undoubtedly been much neglected in the treatment of fractures, and if the book accomplishes nothing more than to again bring this important adjunct of early functional results to the attention of the medical profession, it will have done a good work. The painless treatment and rapid results obtained by the author show what can be done by an expert in this method of treatment, but in the hands of the ordinary physician, it would seem that the patient would have a better chance if a fixation apparatus were used over a longer period of time than is advised in this treatise.

The book is nicely gotten up and is well printed, but the lack of an index is a disadvantage.

The treatment of fractures undoubtedly needs a great deal of improvement, and this book will be of considerable interest to anyone who is endeavoring to develop better methods. Possibly a satisfactory compromise between the generally accepted method and that advocated by the author might solve the problem.

J. S. D.

On Bronchial Asthma. Its Pathology and Treatment. By J. B. Berkart, M. D., etc. Revised and Abridged Third Edition. (*London, New York, etc.: Oxford University Press.*)

The author presents, in this brief monograph, the view on the causation of asthma that it is not of so-called nervous origin, but due to an obstruction of the finer and larger bronchials by a serofibrinous exudation, probably induced by some microorganism. He believes that patients who suffer from asthma have generally a much impaired general nutrition and never have perfectly normal chests, but that these have been affected by rickets in childhood and that as a result, the lungs are usually smaller than the average, though rarely they may be larger. The heart is also affected by these alterations in shape of the chest. The evidence brought forward by Dr. Berkart to support his reasoning does not seem sufficient to explain all cases of asthma, and rather than simplifying the pathology of the disease, makes it more complex in some particulars. It is an interesting theory clearly presented which needs more proof before it can be accepted as the final cause of this obscure disease.

New and Non-official Remedies, 1912. Containing Descriptions of the Articles which have been Accepted by the Council on Pharmacy and Chemistry of the American Medical Association Prior to January 1, 1912. 50 cts. (*Chicago: American Medical Association, 1912.*)

Much praise is due the Council on Pharmacy and Chemistry of the American Medical Association for their careful work in preparing this volume which is serviceable to all physicians as well as pharmacists. The title is self-explanatory. The book is neatly and cheaply printed and in compact form contains the information published weekly by the Council in the Journal of the society. With the abundance of remedies at command it is an outrage that so many physicians should prescribe useless and harmful proprietary drugs, and it is to be hoped that the educational work of this Council and of the association at large will reap greater returns in the future than it has in the past.

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THE EFFECT OF LIGATION OF THE COMMON ILIAC ARTERY ON THE CIRCULATION AND FUNCTION OF THE LOWER EXTREMITY.

REPORT OF A CURE OF ILIO-FEMORAL ANEURISM BY THE APPLICATION OF AN ALUMINUM BAND TO THAT VESSEL.

By W. S. Halsted, M. D.,

Professor of Surgery, The Johns Hopkins University.

The purpose of this paper is not so much to publish a case in which a cure of ilio-femoral aneurism was accomplished by the application to the common iliac artery of a barely or completely occluding aluminum band as to consider the reasons for the view which prevails that ligation of this artery is an exceedingly dangerous procedure and likely to be followed by gangrene, and to determine, if possible, the ultimate result of this operation so far as usefulness of the limb is concerned.

I have endeavored to assemble all the cases of ligation of the common iliac artery reported since 1880, accepting, in order to avoid confusion, this arbitrary date, proposed by Dreist[1] as being within the antiseptic period. Although antiseptic surgery was not universally practiced until after 1890 in the United States and Great Britain, the countries which have contributed most to the surgery of the common iliac and of the other large arteries, infection has not played part enough in the cases here collected to obscure the factors responsible for the results and thus prevent the drawing of deductions concerning the matters which it is the particular purpose of this paper to consider.

In the years from 1880 to 1912, the common iliac artery has been ligated at least 30 times, or about once a year, for the control of hemorrhage and the cure of aneurism.

Undoubtedly the reports of some have been overlooked by me and the number of unpublished cases may be considerable. The Index Medicus has been of the greatest assistance in my search, not one of the cases found in other medical bibliographies having been overlooked by this indispensable work. Only three of the published cases of my list are not to be found in the admirably arranged and marvellously accurate index of the Index Medicus and there is good excuse for the omission of these, there being no titular indication of their existence.

Thanks to the courtesy of Dr. McCaw, the library at Washington of the Surgeon-General has been at my disposition, and not one of the desired articles has been wanting from its shelves. This privilege has enabled me to make an abstract from the original article in every case.

The common iliac artery was ligated for the first time July 27, 1812,[2] *just one hundred years ago,* and in this period it has been tied about 100 times.

The original operation was performed for the arrest of hemorrhage, by William Gibson,[3] at that time Professor of Surgery in the University of Maryland, Baltimore. The patient was a male, æt. 38. A musket ball entering the left side of the abdomen passed through the intestine, opened the left common iliac artery and lodged in the sacrum. Peritonitis developed promptly. On the ninth day a severe hemorrhage occurred. From this time, until the death of the patient, on the fifteenth day after operation, there were repeated hemorrhages.

[1] Deutsche Ztschr. f. Chir., 1903, LXXI, Heft 1, 26.

[2] Am. M. Recorder, 1820, III, 185.

[3] Dr. Gibson performed this operation at the age of twenty-four. It was due to his efforts that, the previous year, the Medical School in which he held the Chair of Surgery was founded.

Valentine Mott was the first deliberately to tie the common iliac artery. The operation, undertaken for the cure of iliofemoral aneurism, was successful. The story of the case as related by him is impressive and gives one some idea of the courage, skill, sagacity and resourcefulness of this remarkable man.

The following passages are quoted from Dr. Mott's report:[4]

"On the 15th of March, 1827, I was requested to visit a patient with Dr. Osborn (of Westfield, New Jersey, about twenty-five miles distant from New York) whom we found laboring under a large aneurism of the right external iliac artery.

"Israel Crane, aged 33 years, says that about the middle of January he felt some pain about the lower part of the belly, which he attributed to a fall received during the winter.

"It, however, was not until a fortnight since, that he perceived any tumor about the lower part of the abdomen. Upon examination, the abdomen on the right side was considerably enlarged from about the crural arch, as high as the umbilicus. When the hand was applied to the parietes of the abdomen a pulsation was felt and rendered visible to some distance. To the touch, the tumor beat violently and appeared to contain only fluid blood. It commenced a little above Poupart's ligament and reached, judging by the touch, from without near the navel—inwards, almost to the linea alba—outwards and backwards filling up all the concavity of the ileum, and reaching beyond the posterior superior spinous process of that bone.

"The rapid increase of this aneurismal tumor occasioned, as the countenance of our patient indicated, the most extreme agony. His sufferings were at times so great that his screams could be heard at a distance from the house. He had been bled several times, taken light food, and was kept constantly under the influence of opium. He was now informed of the serious nature of his case, and that without an operation very little chance of his life remained. With great composure he immediately consented to whatever would give him the best prospect of saving his life.

"From the extent and situation of the tumor, he was apprised of the uncertain nature of the operation, as well as the difficulty of performing it, and indeed that it would require an artery to be tied, which never had been operated upon for aneurism.

"With these views of his situation, he cheerfully submitted to be placed upon a table of suitable height in a room which was well lighted.

"The pubes and groin of the right side being shaved, an incision was commenced just above the external abdominal ring, and carried in a semicircular direction half an inch above Poupart's ligament, until it terminated a little beyond the anterior superior spinous process of the ilium, making in extent about five inches.

"The integuments and superficial fascia were now divided, which exposed the tendinous part of the external oblique muscle, upon cutting which in the whole course of the incision, the muscular fibers of the internal oblique were exposed; the fibers of which were cautiously raised with the forceps and cut from the upper edge of Poupart's ligament. This exposed the spermatic cord, the cellular covering of which was now raised with the forceps, and divided to an extent sufficient to admit the forefinger of the left hand to pass upon the cord into the internal abdominal ring. The finger serving now as a director, enabled me to divide the internal oblique and transversalis muscles to the extent of the external incision, while it protected the peritoneum. In the division of the last mentioned muscles outwardly, the circumflexa ilii artery was cut through, and it yielded for a few minutes a smart bleeding. This, with a smaller artery upon the surface of the internal oblique muscle, between the rings, and one in the integuments were all that required ligatures.

"With the tumor beating furiously underneath, I now attempted to raise the peritoneum from it, which we found difficult and dangerous, as it was adherent to it in every direction. By degrees we separated it with great caution from the aneurismal tumor, which now bulged up very much into the incision. But we soon found that the external incision did not enable us to arrive at more than half the extent of the tumor upwards. It was, therefore, extended upwards and backwards about half an inch within the ilium, to the distance of three inches, making a wound in all about eight inches in length.

"The separation of the peritoneum was now continued, until the fingers arrived at the upper part of the tumor, which was found to terminate at the going off of the internal iliac artery. The common iliac was next examined by passing the fingers upon the promontory of the sacrum, and to the touch appearing to be sound, we determined to place our ligature upon it about half way between the aneurism and the aorta, with a view to allow length of vessel enough on each side of it to be united by the adhesive process.

"The great current of blood through the aorta made it necessary to allow as much of the primitive iliac to remain between it and the ligature as possible, and the probable disease of the artery higher than the aneurism required that it should not be too low down. The depth of this wound, the size of the aneurism, and the pressure of the intestines downwards by the efforts to bear pain, made it almost impossible to see the vessel we wished to tie. By the aid of curved spatulas, such as I used in my operation upon the innominata, together with a thin, smooth piece of board, about three inches wide, prepared at the time, we succeeded in keeping up the peritoneal mass, and getting a distinct view of the arteria iliaca communis, on the side of the sacro-vertebral promontory. This required great effort on our part, and could only be continued for a few seconds. The difficulty was greatly augmented by the elevation of the aneurismal tumor, and the interception it gave to the admission of light.

"When we elevated the pelvis, the tumor obstructed our sight; when we depressed it, the crowding down of the intestines presented another difficulty.

"Introducing my right hand now behind the peritoneum, the artery was denuded with the nail of the forefinger, and the needle conveying the ligature was introduced from within outwards, guided by the forefinger of the left hand in order to avoid injuring the vein. The ligature was very readily passed underneath the artery, but considerable difficulty was experienced in hooking the eye of the needle, from the great depth of the wound and the impossibility of seeing it. The distance of the artery from the wound was the whole length of my aneurismal needle.

"After drawing the ligature under the artery, we succeeded, by the aid of our spatulas and board, in getting a fair view of it, and were satisfied that it was fairly under the primitive iliac, a little below the bifurcation of the aorta. It was now tied; the knots were readily conveyed up to the artery by the forefingers; all pulsation in the tumor instantly ceased. The ligature upon the artery was very little below a point opposite the umbilicus.

"The operation lasted rather less than one hour.

"In less than one hour from the operation, considerable reaction of the heart and arteries took place; he felt, as he stated, altogether relieved from the excruciating agony he had suffered since the aneurism commenced. The whole limb had now recovered its natural temperature.

"March 16. The day after the operation; pulse eighty; skin moist; limb warm as the other; complains of some pain at the ligature; ordered a purgative of neutral salts.

"March 17 and 18. There was considerable pain in the limb.

[4] Successful Ligation of the Common Iliac Artery. By Valentine Mott, M. D., Professor of Surgery, N. Y. Am. J. M. Sc., 1827, I, 156.

"April 8. There are no disagreeable appearances whatever. He appears to be doing remarkably well; has been bled once since the last report; takes a purgative every other day, and an opiate every night; pulse as in health; no pain; says he is entirely comfortable; wound dressed with dry lint.

"April 16. Has improved rapidly since the last report. Two days after the ligature came away he very imprudently got out of bed without experiencing any difficulty, except weakness. Rode out to-day; wound perfectly healed.

"April 30. Is perfectly restored to health; has a little stoop in his walk, which he says is occasioned by the external cicatrix. Leg is not yet of its full size, nor quite so strong as the other. From the period of the operation, to the recovery of our patient, he did not appear to suffer more pain, or to have more unpleasant symptoms, than would ordinarily take place in a flesh wound of equal extent.

"May 29. My patient visited me to-day, having come twenty-five miles; he was so much improved in health that I did not recognize him. Examined the cicatrix and found it perfectly sound; could not discover any remains of aneurismal tumor; *felt the epigastric artery much enlarged and beating strongly* (italics mine), and a feeble, though distinct pulsation in the femoral artery immediately below the crural arch. The leg has its natural temperature and feeling, and he says it is as strong as the other.

"The gratification his visit afforded me is not to be imagined, save by those who have been placed under similar circumstances. The perfect success of so important and novel an operation, with the entire restoration of the patient's health, was a rich reward for the anxiety I experienced in the case, and in a measure compensated for the unexpected failure of my operation on the arteria innominata.

"New York, 25 Park Place, October 15, 1827."

It is interesting to note that Dr. Mott raised the pelvis, just as we do to-day, with the object of having the abdominal contents gravitate towards the thorax. Being without artificial illumination or means of reflecting the day-light into the wound, he had to abandon this useful, and for us to-day, quite indispensable measure because with the pelvis elevated, the aneurismal tumor obstructed the view.

In 1853, Prof. Uhde, of Braunschweig, tabulated 17 cases of ligation of the common iliac artery performed to the year 1850 and reported in full detail a case in which he tied this vessel for aneurism of the gluteal artery. The article is illustrated with interesting wood-cuts depicting the conditions found by him at the autopsy of his patient. Uhde tabulated also, in this paper, the ligations, to 1852, of various arteries for the cure of gluteal anuerism.

Of the statistical papers on the subject of ligation of the common iliac artery the classic one of Stephen Smith,[5] published in 1860, is especially important.

It is a tale of woe that Dr. Smith had to relate, tragic for the patient and for the surgeon; but hardly more pitiful than is to be found in the history of the operation as it has been performed in our modern antiseptic and aseptic times.

Stephen Smith collected 31 cases of ligation of the common iliac artery and reported an additional case of his own. In the 32 years from 1829 to 1859, 32[6] ligations of this artery were made and this average of one a year has been approximately maintained to the present time.

In the following table Dr. Smith has arranged the cases in chronological order (l. c., p. 19).

No.	Date of Operation.		Operator.	Result.
1	July	27, 1812	Gibson, of Philadelphia	Died
2	March	15, 1827	Mott, of New York	Cured
3	July	18, 1828	Crampton, of Dublin	Died
4	December	1, 1829	Liston, of Edinburgh	Died
5	August	24, 1833	Guthrie, of London	Cured
6	April	1836	Stevens, of New York	Died
7	May	26, 1837	Salomon, of St. Petersburg	Cured
8		1837	Garviso, of Monte Video	Died
9	June	8, 1838	Syme, of Edinburgh	Died
10	November	29, 1838	Pirogoff, of Dorpat	Died
11	April	10, 1839	Bushe, of New York	Died
12	February	22, 1840	Deguise, of Paris	Cured
13	August	26, 1840	Post, of New York	Died
14	August	29, 1842	Peace, of Philadelphia	Cured
15	December	3, 1843	Hey, of York	Cured
16		1843	Garviso, of Monte Video	Cured
17	January	27, 1845	Stanley, of London	Died
18	June	3, 1847	Lyon, of Glasgow	Died
19	September	19, 1850	Chassaignac, of Paris	Died
20	December	29, 1851	Jones, of Liverpool	Died
21	January	1852	Moore, of London	Died
22	March	27, 1852	Wedderburn, of New Orleans	Died
23	October	7, 1852	Uhde, of Braunschweig	Died
24	November	1853	Van Buren, of New York	Died
25	March	20, 1857	Edwards, of Edinburgh	Died
26	March	26, 1857	Holt, of Georgia	Died
27	July	15, 1857	Meier, of New York	Died
28	July	3, 1858	Parker, of New York	Died
29	July	6, 1858	Buck, of New York	Died
30	October	6, 1858	Stephen Smith, of New York	Died
31	January	26, 1859	Stone, of New Orleans	Died
32			Goldsmith, Louisville	Died

"The indications," Dr. Smith writes, "which have thus far led to the deligation of the primitive iliac artery may be divided as follows:

"I. For the arrest of hemorrhage.

"II. For the cure of aneurism.

"III. For the cure of pulsating tumors, which proved to be malignant growths.

"IV. For the prevention of hemorrhage in the removal of a morbid growth."

In Group I are eleven cases. Ten of these died; nine from hemorrhage, primary (five), or secondary (four); one from peritonitis. Dr. Smith contrasts the mortality from ligation of the primitive iliac artery for the arrest of hemorrhage (approximately 91%) with that following the same operation performed 14 times upon the external iliac artery for the same causes (21½%) and makes this comment "a proper appreciation of the circumstances under which the primitive iliac artery has been tied for the arrest of hemorrhage will lead the discriminating surgeon, notwithstanding the excessive mortality that

[5] A Statistical Examination of the Operation of Deligation of the Primitive Iliac Artery, embracing the Histories (in abstract) of Thirty-two Cases. By Stephen Smith, M. D., Surgeon to Bellevue Hospital, New York. Am. J. M. Sc., 1860, n. s. XL, 18.

[6] The date of the 32d operation by Middleton Goldsmith was not obtainable, but as Prof. Goldsmith reported it in February, 1860 (Louisville Medical Journal), the operation was presumably performed in 1859, or earlier.

has thus far attended its performance, to accord to this operation an important place among the resources of his art."

In Group II (for the cure of aneurism) there are 15 cases. Five of these recovered; ten died; in two the result was unknown. This group has the greatest percentage of recovery from the operation and it is noteworthy that in at least one, Peace's, of the non-fatal cases, ligation of the common iliac artery did not suffice to cure permanently the aneurism which returned about 14 months later, ruptured and caused the death of the patient. In one of the recovered cases, Salomon's, gangrene ensued as result of the ligation. In this instance, a gangrenous eschar formed on the foot on the third day after operation, and "subsequently others appeared," but "convalescence was complete at the end of two months." This patient died ten months after the operation from an abscess below Poupart's ligament on the operated side.

Gangrene was the cause of death in two of the fatal cases, but in one of these, Syme's, it was present before operation.

Dr. Smith makes the following comment in considering the results of the operation of deligation of the common iliac artery for aneurism, as compared with the same operation upon the external iliac:

> In ninety-five cases, which I have examined, of ligation of the latter (external iliac) artery for aneurism, sixty-nine recovered and twenty-six died, being a mortality of about 27 per cent, or less than half the mortality of the same operation for the same disease when performed upon the common trunk. The cause of death in eleven cases, or nearly one half, of ligation of the external iliac for aneurism was mortification of the limb, presenting a striking contrast with the same operation upon the primitive iliac in which there was but one instance in eight cases.

Group III. *Deligation of the common iliac for malignant tumors simulating aneurism.* It is noteworthy that in all four of the cases in this group the pulsating neoplasm was mistaken for aneurism. Mr. Astley Cooper who saw, in consultation, Mr. Guthrie's case expressed himself as positive that it was an aneurism.

In Group IV are two unclassified cases. The second of these, Chassaignac's, was, as Dr. Smith says, one of the most remarkable of the series. This eminent surgeon operated in a most brilliant manner for the cure of a large encephaloid tumor of the internal and superior aspect of the thigh, extending to the foramen ovale, and after ligation of the common iliac artery, the tumor was removed, "with scarcely the appearance of blood." The entire operation, performed under chloroform, lasted only half an hour.

Surgeons of the present day would be entertained by the perusal of the comments which Chassaignac's report of the case called forth, at a meeting of the *Société de Chirurgie.*[7] Dr. Smith gives an abstract of the discussion. Larrey, Robert and Forget condemned the operation in unqualified terms, Larrey blaming the operator for attempting so considerable an operation without previous consultation with his colleagues. Gosselin and Maisonneuve sustained Chassaignac.

In the 32 cases the extraperitoneal incision was employed by all the operators with the exception of Gibson, Garviso, Post and Goldsmith. Of the nine cases in which the peritoneal cavity was opened, either accidentally or intentionally, only two acquired peritonitis, and in both of these hemorrhage was an associated cause of death.

Another paper of importance on the subject of ligation of the common iliac artery and almost equal in statistical value to Stephen Smith's, is by Kümmel,[8] assistant at that time (1884) of Prof. Schede in the Allegemeines Krankenhaus zu Hamburg, and at present Surgical Director of the Eppendorf Hospital, Hamburg, which is so well known to surgeons throughout the world. To the thirty-two cases of Stephen Smith, Kümmel adds thirty, collected from the twenty-four years between 1860 and 1884, an average of one-quarter of a case per year in excess of the record of the first 32 years in the history of the ligation of this artery.

With one or two exceptions, the complications which have led to the performance of this operation have been of grave import. In Groups III[9] and IV[10] of Stephen Smith they are obviously of such nature as to make the cases comprised in these groups useless for the purpose of this study.

We shall consider, therefore, only cases which have been operated upon for the control of hemorrhage (Group I), or the cure of aneurism (Group II).

ABSTRACTS OF CASES FROM 1880 TO 1912.

1. (Group I.) O'Grady, E. S. *Ligation of the left common and internal iliac arteries to arrest hemorrhage in a case of varicose aneurism for the cure of which the femoral artery had been ligated nine months previously. Death in about seven hours.* (The Medical Press and Circular, Dublin, 1880, July 28, p. 71.)

Male, æt. 28. At the age of 13, patient clapped his thighs together to catch a shoemaker's knife. The sharp knife "transfixed the long saphenous vein and penetrated the femoral artery." Since the accident he had required surgical assistance at various times. With the aid of rest and the habitual use of an elastic bandage he had managed to earn a living. A pulsating tumor had formed "in the anterior and inner region of the middle of the left thigh." When examined by Mr. O'Grady (presumably in November, 1879), this tumor was as large as a cocoanut, and very prominent. From its lower part, there projected two hemispherical nodules as large as walnuts. The tissue intervening between these and the pulsating finger was so thin that it seemed as if the pulsating tumor might burst at any moment. Pressure on the femoral artery above stopped the pulsation. The long saphenous vein, dilated to the size of a man's thumb, "traversed and was imbedded in the mass." "There were enormously large knots of dilated and tortuous veins behind the knee and down the leg." A bruit was distinctly audible to bystanders and could be loudly heard over the heart.

Operation.—(Nov. ? 1879.) Two days after admission to the Mercer's Hospital, Dublin, the superficial femoral, cut down upon, was found to be as large as "a large man's middle finger"; its coats were "thin and unhealthy looking." The vessel was ligated with carbolized catgut in two places and cut between, the upper ligature being about one inch below the origin of the profunda

[7] Bull. Soc. de chir. de Par. Paris, 1851.

[8] Kümmel, Arch. f. klin. Chir., 1884, XXX, 65.

[9] Group III. Ligations of the common iliac for the cure of pulsating, malignant growths.

[10] Group IV. For the prevention of hemorrhage in the removal of a morbid growth.

artery. Each of the divided ends was again tied with a ligature of the same material. The wound was loosely closed with two interrupted sutures and covered with lint moistened in carbolized oil. The limb was wrapped in flannel bandages and surrounded by hot jars. Three hours after the operation the foot and leg were found to be very cold. The following morning they became warmer. The tumor was quite solid. Three days later the wound and parts about it were considerably inflamed, but there was no return of the pulsation or thrill. The latter lessened in intensity, "soon" returned, however, in the long saphenous vein which "stood out large and distended." Attempts, continued for some weeks, to bring about obliteration of this vein by pressure with padded corks proved ineffectual.

"Sixty-six days after the deligation an aqueous solution of perchloride of iron was injected into a carefully insulated portion of the saphenous vein, the region selected being the central two inches where it crossed the tumor." Ten days later the same procedure was repeated without the desired result. But a week later a like injection, made lower down into the vein, was followed by a satisfactory local reaction, which in two days had sprung up and down the vein and "thoroughly coagulated its contents for its entire length."

One hundred and forty-eight days after the operation the patient left the hospital, his departure having been delayed by "recurrent attacks of more or less severe inflammation of the glands of the groin." The vein remained obliterated, and the aneurism was slowly getting smaller. July 5, nine months after the deligation of the femoral artery, the patient returned to the hospital because there had been slight bleeding from the cicatrix. He reported that there had been occasional attacks of inflammation in the groin, and that from a particular spot in the cicatrix there would be discharged, every now and then, a drop or two of thin matter.

Examination.—The right groin and the abdomen to the ribs were swollen and tender and reddened with an erysipelatous blush. There was pulsation in "the stump of the femoral," but the swollen condition of the parts precluded the possibility of recognizing with certainty "how far any fresh aneurism formation might be present."

"On the night of the 8th, it could be determined that an aneurism had formed on the stump of the femoral, and was rapidly increasing in size."

July 9. At 7.45 a. m., "a terrible gush of arterial hemorrhage occurred," which, "though arrested 'on the moment,' left the patient blanched and prostrate."

Two hours later, the patient having rallied a little, the external iliac artery was cut down upon through matted tissues and adherent glands, but the vessel, found to be enormously enlarged, could not be isolated. So the incision was prolonged to the tip of the twelfth rib. The external iliac artery was followed up. It was tortuous and "as big as a sausage," "resembling a coil of intestine." The internal iliac, "atrophied rather than enlarged," was ligated with catgut and the common iliac artery as well.

The patient rallied and complained of great pain along the front of the tibia.

Seven hours later, becoming suddenly pulseless, he died.

Under difficult conditions a local examination was effected. There had been no further bleeding, and nothing was found to account for the sudden demise. "*The external iliac much exceeded the abdominal aorta in size;* it was a marvel how such a river of blood was controlled promptly enough to prevent immediate death." The long saphenous vein was atrophied and impervious.

2. (Group II.) Richter, C. M. *Ligation of the right common iliac for huge aneurism of the external iliac artery. Gangrene before operation.* (Max Richter, Pacific Medical and Surgical Journal, 1880-1881, p. 505.)

Male, æt. 30. Admitted to the German Hospital, San Francisco (?) Jan. (?) 1881. "Rheumatic" pain in right inguinal region six and one-half months before admission.

Examination.—An irregular tumor the size of a child's head occupied the right hypogastrium. Pulsation not discernible. On auscultation a remote bruit could be heard. Arterial blood was aspirated with a hypodermic syringe. The right leg was œdematous, and its circumference about twice that of the other. Sensibility normal. Motility unimpaired. Patient was very anemic, suffered from dyspepsia and constipation and from severe pains in the right leg and sacral region, which recurred every morning. The proposition to ligate the common iliac was not acceded to by the patient for several weeks. The tumor meanwhile increased in size, the pains became more severe, and finally intolerable and uncontrollable by morphia. Power of motion in the leg became lost and signs of gangrene appeared. Finally the patient consented to the operation.

Feb. 19. The right common iliac was ligated by Dr. C M. Richter. On account of the enormous size of the aneurism and the œdema in the tissues about it, the incision was made on the left side, parallel to Poupart's ligament, and the artery exposed extraperitoneally. The artery was tied with a silk ligature about one-half inch from its origin. The aneursim collapsed, but the gangrene, in two days, had extended to the knee. The limb was anesthetic as high as Poupart's ligament. Nowhere in the extremity could arterial pulsation be felt. Three days after ligation, amputation of the thigh was made. The operation was performed according to the antiseptic method of Lister. An Esmarch bandage was applied just below Poupart's ligament, and the amputation performed in a manner quite bloodless. The large arteries were filled with recently coagulated blood. On removal of the Esmarch bandage, vessels bled from all parts of the stump, and twenty or thirty blood-vessels were ligated.

On the ninth day the surface of the stump appeared to be gangrenous. Chloride of zinc was applied, seemingly with good effect. On the thirteenth day afterwards, there was a rise in temperature, but the wound was granulating satisfactorily. Pus was discharged from the abdominal wound on the fifteenth day.

On the thirty-third day after operation, the patient was doing well. The ligature had not yet come away, but ultimate recovery seemed assured.

3. (Group II.) Nicoladoni. *Ligature of the right common iliac artery for spurious aneurism of the right hypogastric region. Death forty-five hours after operation.* (August Sulzenbacher. Wiener medicinische Presse, 1882, Nos. 7, 8, and 9.)

Male, æt. 31. Admitted to the Innsbruck Hospital, Nov. 11, 1881. Four weeks before admission was wounded in the right groin with a knife. Profuse bleeding from the wound was controlled by pressure of the patient's hand until his strength failed; then, with both hands, he pressed the flexed thigh on the body in order to arrest the hemorrhage. In this position the patient was carried to the Bozener Stadtshospital. On arrival, the bleeding had ceased. A wound in the middle of the right inguinal fold, promptly closed with stitches, healed with the formation of a small abscess. Thirteen days later, apparently recovered, he left the hospital, but soon applied for admission, because a tumor had developed in the right hypogastrium, which from day to day increased in size.

Examination (on admission to Prof. Nicoladoni's clinic).—Skin and mucous membrane pale, voice weak and motions strengthless. The right lower extremity, swollen, bent at knee, and hip rotated outwards. The swelling was greatest at junction of thigh and trunk, where the skin was tense and glistening, and the ramifications of the veins dilated. A pulse in the femoral artery could be felt, but it was barely perceptible in the posterior tibial. The entire right hypogastrium was conspicuously vaulted by a hard, and, in places, nodular tumor which extended from the anterior

superior spine to beyond the middle line, and from two inches below the navel into the pelvis behind the symphysis. On palpation, a peculiar vibrating thrill and slight heaving synchronous with the heart's systole could be appreciated. From the rectum a hard tumefaction was felt on the right side.

Diagnosis.—"Aneurysma Spurium; masses of coagulated blood in the pelvis; wound of epigastric artery, probable; of external iliac artery, or of both these vessels, possible." It was emphasized that the femoral artery pulsated peripherally to the seat of the injury.

Operation.—Nicoladoni. Nov. 15, 1881. Long, mid-line incision to give ready access to the large arteries in case of necessity. Then a long incision parallel to Poupart's and, finally, through this ligament in search for the epigastric artery, and to expose the femoral vessels.

On the accidental opening of the sac, a profuse spurting hemorrhage occurred. After a vain attempt to isolate the pulsating external iliac from the wall of the aneurism, the peritoneal cavity was entered and the common iliac artery ligated with iodoformized silk. Thus the pulsation and bleeding were completely arrested. Intestines which had been eventrated to facilitate the operation were replaced and the abdominal wound sutured. Then the femoral artery was ligated peripherally, and the aneurismal sac laid open. In a small cavity, the size of a hen's egg, a hole in the upper side of the femoral (?) artery was found; a second larger cavity led into a wide subperitoneal space. Arterial hemorrhage "from the peripheral end of the external iliac" (?) was controlled by the central ligation of this vessel. Great masses of blood coagula, black and rusty brown in color, were removed from the spurious sac, which extending into the small pelvis and filling the iliac fossa, had dissected down the thigh under the fascia lata and between the muscles. Wound closed, drained and covered with antiseptic dressing. Duration of operation, with deep narcosis, three and one-half hours.

The following day, Nov. 16, pain in leg and, later, in abdomen. Great thirst and restlessness. Pulse 144, temperature 102.

Nov. 17. Death at 10 a. m., forty-five hours after operation.

Autopsy.—Ligature on common iliac, 2.5 cm. below aortic division. Above this point, a soft clot in the artery. Right internal iliac artery decidedly larger than the left. The crural artery together with the epigastric ligated at Poupart's ligament. In the anterior abdominal wall, the epigastric artery had been cut through not far from its origin. The femoral vein was dilated and filled with a tough and adherent thrombus, on removal of which there was found in the posterior wall of the vessel a sharp-edged slit. The femoral artery, united with dense connective tissue to the vein, was found to be again ligated below Poupart's ligament. The stabbing knife had, therefore, cut across the epigastric artery near its origin and into the femoral artery and vein, thus confirming one of the possibilities formulated in making the diagnosis. No reference is made to the condition of the circulation in the foot.

4. (Group II.) Lange, F. *Ligation of the left common iliac artery for ileo femoral aneurism. Cutaneous gangrene of great toe. Cure of aneurism.* (New York Medical Journal, 1883, p. 610.)

Patient, male, æt. 36. Denied syphilis, but had had leutic manifestations. In July, 1882, the patient experienced pain about the left knee, which appeared quite suddenly and caused pronounced lameness for a time. He noticed also a lump about the size of a pigeon's egg in the left groin. Never entirely free from soreness in the knee joint, he suffered at times intensely until January, 1883. The patient was seen by Dr. Lange for the first time in July, 1883. At that time, "a pulsating tumor with all the characteristics of an aneurism occupied almost the whole of the left iliac fossa, causing the abdominal wall to protrude above Poupart's ligament. Its upper boundary ran from the anterior spinous process toward the umbilicus, ending about an inch below the latter in the middle line which formed its mesial outline. A spindle-shaped process of the tumor extended in the direction of the femoral artery below Poupart's ligament. But nowhere could arterial pulsation be detected in the limb, which was cool and had a bluish hue."

Operation.—July 26. Intraperitoneal ligation of the common iliac artery. Silk ligature, ends cut short. "No bad symptoms followed the operation, and the vitality of the limb remained unimpaired, excepting a small cutaneous necrosis of the great toe."

Three months later the temperature of the affected limb had become more nearly normal, but it was paler in color than the other, and was less well nourished. Its sensibility was normal, but its reflex irritability was diminished. The pain had ceased and the tumor had shrunk to the size of an orange. The coolness, numbness and blueness of the leg before operation presaged insufficient collateral circulation.

5. (Group I.) Kümmel, H. *Ligation of the left common iliac, of the external iliac (twice), of the femoral (three times), and probably of the epigastric and circumflex iliac arteries, without gangrene. After, however, the ligation of three similar arteries (presumably profunda, internal circumflex and external circumflex), gangrene supervened. Recovery.* (Verhand. d. Deutsch. Gesellsch. f. Chir., 1883, and Archiv f. klin. Chirurgie, 1884, XXX, 67.)

Male, aet. 21. Following operation, by an unnamed surgeon, for bubo inguinalis on both sides, there occurred a diphtheritic inflammation of the wound of the left groin.

Nov. 26, 1883. (?), four days after the operation, a profuse hemorrhage took place from the eroded left femoral artery. The bleeding was arrested promptly by digital compression and artery clamps. Dr. Schede placed two ligatures of silk on the femoral artery immediately under Poupart's ligament, and divided the vessel between them. He also "tied off certain vessels opening into the artery above the ligatures." (Epigastric and circumflex iliac ?). It was found that perforation of the femoral artery had occurred in two places. The circulation of the leg was completely restored by evening of the day of operation. The energetic use of concentrated solutions of corrosive sublimate arrested the diphtheritic process in the wound, but caused salivation and bloody stools. The symptoms of mercurial poisoning subsided in a few days under appropriate treatment.

Nov. 30. Severe hemorrhage from the central end of the femoral artery. Although the bleeding was promptly checked with digital compression by an orderly, and then by artery clamps applied by Dr. Kümmel, the loss of blood was badly tolerated by the already greatly reduced patient.

Having transported the patient to the operating room, Dr. Kümmel ligated with catgut, extraperitoneally, the external iliac artery, believing it wiser to operate at some distance from the infected wound, and having found it impossible to make the ligation in loco. On removing the artery forceps, which had been applied to check the hemorrhage from the femoral artery, there spurted forth a stream as powerful as before. Attempts to ligate the femoral (central end) proving again futile, the external iliac was tied once more, just below its origin from the primitive iliac, but without the least influence upon the bleeding. Hence the common iliac was ligated (with catgut, extraperitoneally) about 3 cm. above its bifurcation. Thereupon the bleeding ceased completely. Throughout the operation the wound was almost continuously irrigated with a solution of bichloride of mercury (1-1000), and occasionally flushed with basins full of the same solution. Sev-

eral thick, glass[11] drains were carried down to the site of the ligature on the common iliac; the wound was stitched and dressed with glass-wool and sublimate gauze.

The patient was in the highest degree exhausted by the operation. Puse 120 and thread-like. The left lower extremity quite cold. On the following morning, however, the circulation of the limb was completely restored. Thus *ligation of the common iliac after double ligation of the femoral, double ligation of the external iliac, and ligation, supposedly, of the circumflex iliac and epigastric vessels had not apparently impaired the circulation of the limb, notwithstanding the greatly exsanguinated and exhausted condition of the patient.*

Needle pricks were well perceived and accurately located. Motility was unimpaired. Severe pains in the limb were ameliorated by injection of morphine.

The second day after operation (Dec. 2) the condition of patient and wound were relatively excellent. Pulse 96. The circulation, sensibility and motility of the limb normal. The pains had become much less.

Dec. 10. Ten days after the ligation of the common iliac, there came a sudden hemorrhage from the original "ligature wound" of the femoral. Although the bleeding was promptly controlled by compression of the abdominal aorta and of the bleeding point, the loss of blood was great and the patient utterly exhausted. On closer investigation, it was found that the hemorrhage came from the peripheral end of the femoral. With difficulty isolated from the disintegrated tissues, this was tied off 2 cm. below its divided end. But the bleeding remained unchecked. It came from "three thin-walled arteries about the size of a pen-quill, which ran backwards, inwards and outwards." Were these, perhaps, the profunda, internal and external circumflex arteries?

The following day (December 11) a livid discoloration of the foot was observed. Temperature 105° F. Pulse 144, dry tongue, delirium.

Dec. 12. Pulse 156. Increase of delirium. Livid discoloration to the middle of the leg. Condition of patient so bad as to contraindicate operation.

Dec. 13. The gangrene seemed demarked between the upper and middle thirds of the leg. Pulse 128. A transcondyloid amputation was made as expeditiously as possible, and then a reablation at a higher point on account of the impaired circulation in the flaps. Blood flowed from the femoral artery and vein, and also from muscular vessels. Gradually, the patient developed the picture of a chronic pyæmia. Abscesses appeared on the nates and left arm. Decubitus developed over the sacrum, and in the articulations of the lower jaw and knee. Ultimately, the patient was put in the permanent bath, in which the wound took on a healthy appearance and showed a tendency to heal. From this time the prolonged convalescence was uninterrupted.

March 3. Patient was able to leave his bed.

This case and Clark's (26) are the only ones in the antiseptic period which have recovered after ligation of the common iliac for the control of severe hemorrhage. In the whole literature of the subject there is perhaps no case more thrilling. In our collection of thirty cases of the antiseptic period only eight belong to Group I. Of these, four died, and one (Kümmel's) narrowly escaped death. Of the remaining three, Czerny's belongs only technically to Group I, for the ligation of the common iliac was made in the course of an operation for the removal of tuberculous glands to control slight bleeding from some artery torn off close to its parent trunk in the course of the dissection.

[11] Dr. Kümmel, it will be recalled, was the originator of the *Inorganischer Verband.*

In Meyer's case, very briefly reported, it is not stated that the hemorrhage was severe.

The hemorrhage in Clark's case, however, was to the point of collapse.

6. (Group II.) Schönborn, Karl. *Ligation of the right common iliac for aneurism of the internal and external iliac arteries. Recovery. Cure of the aneurism.* (Stetter. Zentralblatt f. Chirurgie, 1884, p. 160.)

Male, æt. 75. Difficulty in walking beginning in January, 1882, gradually increased until, in October of the same year, patient was unable to step on his right foot. About this time, there was noticed in the region of the right groin a tumefaction which rapidly increased in size, and was at first considered to be an abscess having origin in a bone of the pelvis.

In January, 1883, an aspirating needle was introduced through which "neither blood nor pus" escaped. As the swelling increased, it manifested itself in the gluteal region. At last the pain became so great that there was no relief night or day, except with the use of chloral or morphine.

Examination.—Patient seemed robust for his years, and his general condition was good. He could bear no weight on his right foot, nor walk at all without firm support. Heart and palpable arteries were apparently normal. In the right iliac fossa a strong pulsation could be felt. On careful inspection a slight swelling was observed in the right supratrochanteric region which, fading off towards the right groin, extended behind and below the lower edge of the gluteal musculature. Above, it approached the crest of the ilium, and inwards the pubic symphysis. Throughout its entire extent, rhythmic pulsation could be seen and felt. On auscultation a systolic bruit isochronic with the pulse was heard. In the posterior tibial artery a distinct pulse could be felt. Examination by rectum revealed nothing anomalous.

Diagnosis.—Aneurism in the neighborhood of the common iliac, quite surely of a large vessel, probably of the internal and also of the external iliac. Ligation of the common iliac artery was determined upon as nothing less formidable could be done with any prospect of success.

Operation.—May 2, 1883. Prof. Schönborn. Thymol spray. An incision, 34 cm. long, concave upwards, was made from the inner third of Poupart's ligament to the lower border of the twelfth rib. The artery, exposed in the extraperitoneal manner, had an astonishingly transverse course, and was acutely bent on itself. Its wall seemed softened. A catgut ligature was applied. It developed, on further examination, that the aneurism had its origin in the right hypogastric (internal iliac), and extended over into the external iliac artery. Both vessels gave evidence everywhere of atheromatous changes. At the moment of tying the ligature the rate of the pulse was increased from 60 to 75, and in three minutes, to 80 beats.[12] There was complete arrest of pulsation in the arteries peripheral to the ligature. The ends of the ligature were cut short, drains carried to the artery and elsewhere, the wound was sutured and covered with a Lister dressing. Notwithstanding the precautions, the wound broke down and suppurated everywhere, except at the ends and about the ligature. Necrosis of the fascia and skin necessitated numerous incisions and drainage.

The ligation exerted no manifest influence upon the limb except the blocking of the pulse. The temperature of the skin of the foot, which seemed slightly less than on the opposite side for ten days, remained normal thereafter.

Pains in the extremity were severe at first, but gradually dis-

[12] Compare with observation in Fluhrer's case in which the heart's action was slowed.

appeared altogether. The healing of the wound was slow, accompanied by fever and the separation of necrotic masses.

Aug. 2. Three months after the operation, the wound was healed and the patient discharged. The aneurismal swelling had become considerably smaller. Pulsation neither in it nor in the posterior tibial was to be felt.

Nov. 1883. Six months after the operation patient stated in a letter that he was quite well, and able to walk with a cane.

7. (Group I.) Kümmel, H. *Aneurism of the right inguinal region and the calf. Ligation of the external iliac. Secondary hemorrhage. Ligation of the right common iliac. Death in twelve hours.* (l. c., p. 103.)

Female, æt. 21. Admitted to the medical division of the hospital for articular rheumatism and peliosis rheumatica. Developed aortic stenosis and insufficiency. In the further course of the disease a pulsating tumor, the size of a walnut, and causing great pain, appeared in the right groin in the region of the anterior crural nerve; a short time thereafter, a diffuse, tense, pulsating swelling in the muscle of the calf was observed. For both the diagnosis of aneurism was made.

The condition of the patient was so bad that an operative procedure was not contemplable, especially as the multiplicity of the aneurisms indicated general arterial disease.

The patient's strength continuously failing, there occurred a rupture of the aneurism in the calf followed quickly by extensive gangrene of the soft parts of the leg.

Dec. 5, 1883. The skin and the disintegrated tissues underlying it gave way and, thereupon, there followed a severe hemorrhage. Although this was controlled by a promptly applied Esmarch bandage, the already exhausted patient became almost pulseless as she was brought to the operating table.

As it was impossible to check, in loco, the bleeding, there remained only the alternatives of amputation above the knee or ligation of the main arterial stem. Amputation seemed too serious a procedure. Furthermore, it was feared that rupture of the aneurism in the groin might be brought about by ligation of the femoral artery below it. Hence the external iliac was ligated above the upper aneurism in order to cut the circulation off from this as well as from the ruptured tissues in the calf. Pulsation in the groin ceased, and the aneurismal sac collapsed completely. On removal of the Esmarch bandage, there was no return of the bleeding in the leg. Masses of clots and necrotic tissue were removed from the calf, and the great hole cleaned out and stuffed with sublimate-gauze. In two hours, there was sudden profuse bleeding from the calf and, coincident with this, a tense refilling of the aneurism above, and reappearance of its pulsation.

Again, and in worse condition than ever, the patient was placed on the operating table. The common iliac was ligated extraperitoneally, with catgut, about 3 cm. below the aortic bifurcation. The operation was performed in 15 minutes and without anesthetic. Infusion of 800 cc. of salt solution. Death in 12 hours.

Autopsy.—Aneurism of a branch of the profunda. The posterior tibial artery emptied into the gangrenous cavity of the musculature of the calf. A small aneurism of the right posterior cerebral artery. Insufficiency and stenosis of the aortic valves, and in lesser degree of the mitral.

This case has no bearing on either the mortality or the occurrence of gangrene after ligation of the common iliac. Hemorrhage, unpreventable in an already exhausted patient, was the immediate cause of death.

8. (Group I.) Gouley, John W. S. *Ligation of the right common iliac for diffuse aneurism of the external iliac artery. Death from pyæmia on the twenty-first day. Beginning gangrene.* (New York Med. Jour., 1885, Feb. 28, p. 239.)

Male, æt. 22. Admitted to Bellevue Hospital, New York, Oct. 8, 1871, for a painful pulsating tumor of the right inguinal and iliac regions.

History.—About two years before admission a heavy barrel rolling against him inflicted a contusion in the neighborhood of the right groin. Soon after this injury he contracted urethritis and a chancre. These were followed by an enlargement of an inguinal gland which subsided without suppuration. No constitutional symptoms ensued so far as could be ascertained.

Nine months before entering the hospital he had noticed a tumor just above Poupart's ligament on the right side. Three months later he observed for the first time that it pulsated. It was then about as large as a hen's egg. The man continued to work at heavy labor, although the tumor was rapidly increasing in size and gave him great pain, of a burning character, and chiefly in the course of the anterior crural nerve.

Examination.—There was a large, pulsating, elastic tumor which extended six inches above and two inches below Poupart's ligament, and to within two and one-half inches of the median line. Over it a bellows murmur was distinctly heard. The integument overlying the swelling was dark colored and œdematous. It was thought that slight pulsation could be felt in the right anterior tibial, but not in the femoral or posterior tibial arteries.

Operation.—Oct. 12, 1871. A curvilinear incision, nine inches long, beginning above at the tenth rib, was carried through all the structures of the abdominal wall except the peritoneum. This was reflected upwards, and the spatula which had been used as retractor by Valentine Mott in the performance of the same operation was on this occasion held by Dr. A. B. Mott, his son, who assisted Dr. Gouley. The Mott artery-needle was also employed to carry the stout silk ligature with which the common iliac was tied. Pulsation in the tumor immediately ceased. The operation required only thirty-two minutes.

Oct. 13. The tumor had softened and the pain vanished. The temperature of the limb on the operated side was found to be higher than on the other.

Oct. 14. During the night the patient had a sudden attack of diarrhœa. This was checked by morphia.

Oct. 16. Pulse 112; temperature 102.7° F.

Oct. 17. "The tumor began to show signs of rupture"; its wall at the lower portion had become extremely thin and the overlying integument gangrenous.

Oct. 22. "Dark tarry blood began to ooze from the sac through a small opening, and the sac was floating, as it were, in a pool of pus."

Oct. 26. Pulse 120; temperature 102° F. Dr. Gouley "cut short the slow spontaneous enucleating process by introducing a finger and sweeping around that part of the sac which was out of sight, and at the same time removed portions of sloughy muscular tissue." After the sac had come away he could "with the finger still in the cavity, feel the bladder."

April 27 and 28. Chills and bed-sore. Placed on water-bed. Pulse 140; temperature 103° F.

Oct. 29. Patient complained of intense pain in the heel and foot of the affected side. Sensation was absent in these parts, and their surface was cold.

Oct. 31. Ecchymosis observed about the right ankle. The pain had extended up into the leg and was very intense. Chills.

Nov. 1. "The ecchymosis had greatly increased."

Nov. 2. Death.

Autopsy.—"The ligature lay loose in the wound. The primitive iliac artery was completely obliterated. Nearly the whole of the external iliac had sloughed away with the sac, leaving less than an inch of its lower extremity, which was entirely closed. There was a pelvic abscess which involved the psoas muscle. The femoral and iliac veins were free from thrombus."

Epicrisis.—Dr. Gouley made the following wise comment: "It seems to me that if I had carried out my intention of freely opening the sac, the chances of recovery would have been greatly increased, and that this procedure for which we had such strong warrant, and which in itself is so simple, so philosophical, and therefore so eminently surgical, should be more insisted upon than it has been of late years." The patient "succumbed from pyæmia solely because a great bag of dead decomposing blood was retained in his flank. If after ligature of the main artery the sac had been freely opened and the clots extracted, and the cavity filled with lint, I am sure that the risk of this expedient would have been infinitely small as compared with the expectant plan which was so unfortunately adopted."

The signs of gangrene (ecchymoses) which developed just before death were due, of course, in part to the enfeebled action of the heart, and probably also to the blocking of important anastomotic arteries communicating with and in the immediate neighborhood of the necrotic sac.

9. (Group II.) Jameson, L. S. *Ligation of the right common iliac for aneurism of the external iliac artery. Recovery. Cure of aneurism.* (Lancet, Lond., 1886. March 6, p. 444.)

Female, æt. 28. Admitted to Kimberly Hospital, Cape Colony, April 20, 1885.

Eleven months before admission she noticed a small swelling the size of a nut in the right groin. This gradually enlarged during the following six months, without causing pain, to the size of an apple. Then, the tumor enlarging rapidly and becoming softer, she noticed a "beating" sensation in the swelling, and pain and numbness down the leg.

Examination.—Above Poupart's ligament was an oval pulsating swelling as large as the head of a new-born child, which extended outwards to within an inch of the anterior superior spine, inwards to the mid-line and upwards to the umbilicus. The upper portion of the tumor was solid; below it was soft; the skin of a deep purple color, looked as if it might rupture on the slightest provocation. There was marked swelling of the whole of the right limb. Pulsation in the posterior tibial artery was "practically" imperceptible.

Operation.—April 21. The tumor was so large that it was deemed impossible to expose the right common iliac by operating on the right side. The incision, consequently, was made on the left side; the left common iliac was located extraperitoneally and traced up to the bifurcation of the aorta. The right common iliac, well overlapped by the aneurism which apparently had its origin in the external iliac, was ligated with stout carbolized silk. Pulsation in the aneurism ceased at once.

The following day, April 22. Slight pain and restlessness. Temperature a. m. 101° F.; p. m. 101.6° F. The wound showed increased discoloration at its lower part.

April 23. Discharge of bloody serum from wound. No pain. No abdominal distension.

April 28. Temperature 99° F. No pain. Superficial and deep stitches removed. Some gaping of the superficial wound.

April 29. Pain in the leg. Temperature normal.

May 12. Bed sore over sacrum, which was present on admission. Patient remained in the hospital for three months longer, the tumor diminishing slowly in size.

Oct. 15. On deep pressure the tumor, quite solid, measured 2½ x 3 inches. Both the knee and the hip were considerably flexed, and patient got about with difficulty. Her health was perfect.

The operation was performed, presumably without antiseptics, for Mr. Jameson seems to have acted on the suggestion given him seven years before, as he was about to depart for Cape Colony, not to supply himself with them. Mr. John Marshall had said to him, "You are going to an antiseptic climate and don't require them." Mr. Jameson remarks that this opinion had since been fully justified. Grave injuries, such as compound fractures, which in London would have made amputation imperative, healed at Cape Colony in a marvellously short time under some simple wet dressing, such as boracic lint.

10. (Group II.) Fluhrer, W. F. *Transperitoneal ligation of the left common iliac artery for aneurism of the external iliac.* Death on the seventh day from acute nephritis. (New York Med. Record, 1886, Oct. 26, p. 454.)

Male, colored, æt. 35. Admitted to Mount Sinai Hospital, May 3, 1886.

Four years before admission patient contracted syphilis. In September, 1885, he observed that the left lower limb and groin became "suddenly swollen and painful." Once the swelling in the groin was so great that he could hardly flex the thigh. Since then the swelling diminished, but at no time did it disappear.

Ten weeks before admission, the patient noticed a small, deeply seated pulsating tumor in the left groin. This steadily increased in size and in the force of its pulsations. The patient had lost twenty pounds in weight. He appeared to be only fairly vigorous.

Examination.—The tumor in the left groin was hardly noticeable on inspection, but on palpation it was found to be about two-thirds the size of a fist. From Poupart's ligament it extended upwards to a point about midway between the symphysis and the umbilicus; inwards it reached almost to the mid-line. Its pulsation was expansile, and accompanied by a faint systolic bruit. Pulsation in the left femoral artery, weaker than in the right, could be felt. The circulation of the limb on the affected side was good. There was no visible dilatation of the veins. The visceral examination revealed nothing abnormal. The urine's specific gravity was 1020, and in other respects it was normal.

Diagnosis.—Aneurism involving the whole extent of the external iliac artery.

The Operation (May 20) was conducted with thorough antiseptic precautions. The common iliac artery was tied off about one-quarter of an inch below the bifurcation of the aorta with a silk ligature, which had been boiled for two hours in a 5 per cent solution of carbolic acid. About one minute after the ligation a slowing[13] of twelve or fifteen beats was observed by Dr. Purroy, who was taking the radial pulse. Patient reacted well from the operation which had required two hours.

May 21. He complained of pains in the toes of the left foot. The circulation was "returning in the three lower toes." The urine contained albumen, hyaline casts, and some blood corpuscles.

May 23. The circulation was "good in the foot and toes." A pulse could be felt in the dorsalis pedis artery. Patient was restless. Urine was heavily charged with albumen, and contained hyaline casts in great numbers, and some blood corpuscles.

May 24. Pulse 140; temperature 102.6° F.

May 26. Patient's condition was grave. He was sluggish and unable to swallow.

May 27. Delirium. Died at 1 p. m.

Autopsy.—The abdominal wound had healed by first intention. The aneurism extended the whole length of the external iliac artery. The sac showed a tendency to form pouches. It was filled with a solid clot. The femoral vein was plugged with a firm, hard thrombus. The external iliac vein was impervious and lost upon the surface of the aneurism. "This condition of the veins accounts for the comparatively sudden œdema of the lower extremity and groin in the early history of the disease." The ligature had been applied three-fourths of an inch from the

[13] Compare with Schönborn's case in which the pulse was accelerated fifteen to twenty beats on tying the common iliac.

aneurism and one-fourth of an inch below the bifurcation of the aorta, and precisely at the point of crossing of the ureter. The common iliac vein lay exactly behind the artery. There was an aneurism of the aorta which began at the bifurcation and extended upwards for four inches. Calcified plates could be felt in the walls of the aneurism. In the sac was a clot which contrasted strongly with that which filled the aneurism of the external iliac. The former was pale, firm, laminated, and appeared adherent in places to the wall of the sac; it did not wholly obstruct the lumen of the aorta. "The remaining operative conditions," wrote Dr. Fluhrer, "that favored the development of nephritis were the prolonged and complete anesthetization and *the change in the renal circulation.*" (Italics mine.) "If the shutting off of the main arterial blood supply to one-fourth of the body caused such a disturbance of the general circulation as to be noticed by a slowing and increase in the volume of the radial pulse, surely there must have been a more intense effect upon the renal circulation, not only from the nearness of the renal arteries to the place of ligation, but also from the presence of the clot-containing aneurism of the aorta reaching to within two inches of their origin, which must have been an obstacle to the free delivery of blood to the lower channels." [13a]

11. (Group II). Smith, Thos. *Ligature of the right common iliac artery with kangaroo tendon for a large fusiform ileo-femoral aneurism; yielding of the knot; re-ligature with silk; gangrene of the limb.* (Trans. of the Clin. Soc. of London, 1887, XX, 29.)

Male, æt. 52. Admitted to St. Bartholomew's Hospital, Oct. 14, 1885. An aneurism of the right external iliac artery extended from a point midway between the umbilicus and crural arch into the upper part of the thigh. The right thigh was much swollen, measuring 3 inches more than the left.

Oct. 22. Ligation of the common iliac artery just above the aneurism with kangaroo tendon. The vessel at the point of ligature was very large, and erroneously supposed to be the external iliac. The ligature was cut short and the wound drained.

Oct. 23. Pulsation, as forcible as before the operation of the previous day, returned in the aneurism. Fearing that the knot had slipped, the wound was opened and the common iliac re-ligated with two ligatures of carbolized silk. The knot of the original ligature was not obviously loose, but the point of an aneurism needle could be inserted between the kangaroo tendon and the vessel. The silk ligatures were cut short and the wound drained.

Oct. 24. "No pulsation in the sac. Leg warm, but darkish in color."

Oct. 25. "Pulsation evident in sac; leg mottled and purple . . . colder and insensible; thigh discolored."

Oct. 26. "Pulsation in the sac increasing; condition of the whole limb much improved, as regards color and temperature." Was this perhaps due to the fact that the circulation in the aneurism was being restored?

Oct. 27. "Pulsation in the sac continues, a slough forming in the calf."

Oct. 28. "Pulsation continued in sac, leg and foot becoming blue. Pulse 120; temperature 103° F."

Oct. 30. "Gangrene seems limited to foot and front part of leg; sac still pulsates."

Oct. 31. "Pulsation in sac less, and signs of a line of demarcation; patient's general condition a little better."

"During the next two days the line of demarcation became evident, and on November 2 amputation was performed just above the codyles."

The patient died November 3.

Autopsy.—"No general peritonitis, but some matting of the coils of intestines in the immediate neighborhood of the wound." Thrombosis of the external iliac, common femoral and profunda veins, and of the internal iliac, common femoral, superficial femoral and profunda arteries. The sac of the aneurism was quite filled with a firm laminated clot.

12. (Group II.) Lucas, Clement. *Transperitoneal ligation of the common iliac artery for aneurism of the external iliac.*" "*Successful.*" (Brit. Med. Jour., 1892, Nov. 26, p. 1163. W. Mitchell Banks.)

Mr. Banks makes the following brief reference to a case of Mr. Clement Lucas: "Mr. Shileds' letter is obviously eliciting the necessary experience, as evidenced by Mr. Clement Lucas' communication, in which he reminds us of his successful case of ligature of the common iliac *through the peritoneum* for aneurism of the external iliac artery done three and a half years ago."

13. (Group I.) Meyer, Willy. *Ligation of the common iliac artery for secondary hemorrhage incident to ligation of the internal iliac arteries for enlargement of the prostate gland. Recovery.* (Annals of Surgery, 1894, XX, p. 44.)

Male, æt. 55, admitted to the German Hospital, New York, October, 1893, for enlargement of the prostate gland.

Oct. 5. Ligation of both internal iliac arteries (Bier), extraperitoneally, by Dr. Meyer. In the act of dividing the sheath of the left internal iliac, the point of the scalpel pricked the artery. The Hemorrhage was checked by the finger of an assistant on the common iliac, while Dr. Meyer ligated the artery above and below the wound in the vessel. He then divided the internal iliac between the ligatures. The hemorrhage ceased, but "suddenly it again set in in a most alarming way." The common iliac being once more compressed by an assistant's finger, it was seen that the ligature (catgut) had slipped from the proximal stump of the internal iliac. "Further attempts at properly placing a ligature proving futile, and bleeding continuing," a long artery clamp was placed on each end of the divided vessel. These were allowed to remain in the wound, being carefully packed about with gauze.

The operation on the right side was greatly facilitated by the Trendelenburg position. The right internal iliac was tied in two places with ligatures of catgut, and the artery was not divided. This wound was closed, layer by layer, without drainage.

On the fifth day, the clamps on the stumps of the left internal iliac were removed. The sutured wounds had healed throughout, the track of the forceps, of course, excepted.

"On the evening of the twelfth day, the patient suddenly noticed a hot feeling on the left side; secondary arterial hemorrhage had set in." Compression was promptly made by a well-trained nurse, then by the house surgeon who introduced his finger into the depths of the bleeding canal, and awaited the arrival of Dr. Meyer, who had been summoned. The patient was placed in the Trendelenburg posture, and the wound opened. Dr. Meyer found to his surprise that the bleeding came, not from the internal iliac, but from a hole in the external iliac artery. There was a defect, evidently caused by the pressure of a forceps,

[13a] I quite concur with this conclusion of Dr. Fluhrer as to the possible effect upon the function of the kidneys of obstruction of the arterial circulation below the renal arteries, and would refer the reader to a recent article by my former assistant, Dr. Gatch (Annals of Surgery, July, 1911, liv., p. 30), in which this question is considered. We observed in two cases that partial occlusion of the aorta in the human subject exerted a sudden and profound effect upon the renal findings. Dr. Gatch's careful study of these cases stimulated him to make experiments upon dogs and to determine the effect upon the kidneys of aortic obstruction in the healthy animal.

in the anterior wall of this vessel just below the bifurcation of the primitive trunk. So the external iliac was ligated below the hole, and the common iliac above it. The catgut ligatures cut through the latter twice, and hence a ligature of silk was applied close to the bifurcation of the aorta.

"Soon after the operation, gangrene of the toes and a part of the metatarsus developed, which later necessitated irregular amputation of the anterior part of the foot." The wound of the foot being healed, the patient began to walk about and left the hospital April 28.

So far as reduction in the size of the prostate, and the restoration of the function of the bladder were concerned, the result in the opinion of Dr. Meyer was "encouraging in the extreme." No mention is made in the report of pain in the limb following the ligation of the common iliac, nor is there any note concerning the function of this member.

14. (Group II.) Stevenson, W. F. *Transperitoneal ligation of the left common iliac for diffuse traumatic aneurism of the external iliac and femoral arteries. Recovery. Cure of aneurism.* (Lancet, London, 1896, Jan. 25, p. 224. Brigade-Surgeon-Lieutenant-Colonel W. F. Stevenson and Surgeon-Major H. I. Michael.)

Patient, æt. 35, was a sergeant in the artillery stationed at Dover Castle. About Oct. 12, 1895, patient slipped and fell with his left leg under him. He felt, at the time, a sharp pain in the left groin, but remained on duty for a week. Admitted to hospital, Oct. 19, 1895.

Examination.—The left leg was swollen and œdematous, and the superficial veins were distended. There was a large, forcibly pulsating swelling in the left groin extending from one inch above Poupart's ligament to six inches below it, and occupying almost the entire space between the anterior superior spine to the pubes. Patient was put to bed, his limb elevated and bandaged from the foot to the middle of the thigh.

Oct. 29. The tumor had become larger and was very painful. It was decided, on consultation, to ligate the common iliac on the following day. But on the thirtieth it was found that the tumor had become solid, and that the pulsation had almost ceased.

Nov. 4. No pulsation could be felt, although a faint bruit was still to be heard at a spot over the inner side of the swelling. The leg was much reduced in size, and its temperature was "fairly good." Apparently spontaneous cure was taking place and the collateral circulation being established.

Nov. 14. Slight pulsation had reappeared.

Nov. 15. The picture had entirely changed. Strong pulsation could be felt all over the tumor, which had enlarged in every direction. The local condition was much the same as on admission to the hospital.

First operation.—Aseptic precautions. Mid-line incision. Intestines were lifted out of the abdominal cavity. Ligation, with silk, of the left common iliac artery. Wound closed. Horse-hair suture of the skin. Pulsation in the tumor ceased on tying the ligature. It was the operator's intention to continue the operation in order to turn out the clots from the sac; but as the light was bad and the tumor flaccid, further operative procedure was deferred. The patient made an uninterrupted recovery from the laparotomy, his temperature at no time being above 99° F. The circulation in the limb was unimpaired. The tumor slowly diminished in size; the skin over it became loose and wrinkled. There was no return of the pulsation.

Second Operation.—Dec. 21. Two and a quarter pounds of soft blood clot were removed from a huge cavity in the upper, inner aspect of the thigh, extending from the bifurcation of the common iliac artery to the central end of Hunter's canal. There was so little hemorrhage during this operation that only one ligature was required. The cavity was packed with iodoformized gauze, and allowed to heal by granulation. The circulation of the leg was unimpaired.

15. (Group II.) McBurney, Chas. *Ligation of the left common iliac artery for aneurism of the external iliac. Recovery. Cure of aneurism.* (Annals of Surgery, 1898, XXVIII, 128.)

March 9, 1898. At a meeting of the New York Surgical Society, Dr. McBurney presented a young man, who, the year before, after lifting a heavy weight, felt a pain in the neighborhood of the left groin. A few weeks later he noticed a lump in that region, which gradually increased until it attained the size of a closed fist.

Examination.—The circulation in the limb of the affected side was good. The tumor presented all the characteristics of an aneurism. It terminated below at Poupart's ligament. It was decided that the ligation of the common iliac was indicated. This operation was performed December 18, 1897, transperitoneally, and through a long median abdominal incision. In order to reach the vessel it was necessary to lift out the intestines. On tying the double catgut ligature, pulsation in the aneurism ceased, and the sac rapidly diminished in size. The wound healed by first intention. There were not at any time signs of disturbance of the circulation of the limb. The patient was discharged one month after the operation. He was able to work, but still complained of some weakness in the left leg three months after the operation. There had been no return of the pulsation.

Dr. McBurney's report of the case is very brief. No mention is made of pains in the leg, in the days immediately following the operation.

16. (Group II.) Bryant, Jos. D. *Ligation of the right common iliac artery for aneurism of the external iliac. Died in three days.* (Annals of Surgery, 1898, XXVIII, 128.)

In the discussion of McBurney's case, Dr. Bryant stated that about five years before, at St. Vincent's Hospital, he ligated the right common iliac for the cure of a large aneurism of the external iliac artery, which had been present for a long time and caused the patient great distress.

He experienced some difficulty in locating the artery, as it was displaced considerably to the right side. On account of the anomalous position of this artery the left common iliac, correspondingly misplaced, narrowly escaped the ligation. The patient was in bad condition, and survived the operation only three days.

"At the autopsy it was found that the aorta rested and bifurcated on the right instead of the left side of the lumbar vertebrae." This anomaly, Dr. Bryant said, occurs in about 5 per cent of the cases.

17. (Group II.) von Büngner. *Ligation of the left common iliac artery for aneurism of the ischiadic artery. Excision of sac, gangrene.* Death. (R. v. Varendorff. Ueber die Verletzungen und Aneurysmen der Arteria glutea und ischiadica. Inaug. Dissertation, Marburg, 1899.)

Female, æt. 66, admitted to the Landkrankenhaus, June 11, 1898.

Anamnesis.—Suffered from rheumatism ten years ago, and since then from varicose veins and ulcers of the leg; otherwise, has always been well.

In November, 1897, she noticed, on placing her hand upon the left hip, a very distinct pulsation and heaving under it. Since that time a swelling forming in the gluteal region has been slowly but appreciably increasing in size, and assuming more and more the hemispherical form. Presently pains were felt starting in the tumor and radiating down the back of the thigh to the toes. Finally the pains became so severe as to be uncontrollable by morphia.

For the past few weeks she could lie only on the unaffected side, and with thigh and knee slightly flexed.

Status præsens.—Large, robust woman. Area of cardiac dullness slightly increased to the left and right. A blowing, mitral,

systolic murmur. The second pulmonary sound accentuated. Atheromatous arteries. Pulse 88-96, small and soft. Urine normal. Highly developed varices. Scars of healed leg-ulcers. On the left buttock is a tumefaction as large as the hand of a child which, synchronous with the pulse wave, rhythmically rises and falls. The tumor is 23 cm. high by 19 cm. broad. With the hand one feels very distinct pulsations, and constates that these do not become stronger when the tumor is pressed into the buttock. The tension in the tumor is so great that fluctuation can hardly be made out. A swishing bruit is to be heard everywhere over the tumefaction. Pelvic examination negative.

Diagnosis.—Spontaneous aneurism of the gluteal or sciatic artery; mitral insufficiency; general arteriosclerosis.

Operation.—June 14, 1898. (Prof. v. Büngner.) Patient on her right side. Aneurism when exposed was blue, very tense and strongly pulsating. In the endeavor to tie all the arteries leading to the aneurism (Philagrius) a little tear in the sac wall was made, and through this there spurted a powerful stream of blood. The hemorrhage was checked by the pressure of a finger. Attempts to close the hole with suture and forceps were made in vain, and always attended with great hemorrhage. So the finger pressure had to be relied upon while the operation for the ligation of the common iliac artery was being conducted, the right-sided position of the patient being continuously maintained.

This position was found to be so advantageous for the exposure of this artery that v. Varendorf urgently recommends it as greatly facilitating the performance of this operation. The external and common iliac arteries were plainly visible. The internal iliac which could be felt and, in its central portion, seen was found to be the seat of a fusiform aneurism throughout its entire length. Fearing to apply a ligature to an artery so diseased, the common iliac was tied as the only alternative. Immediately the pulsation and thrill ceased in the gluteal aneurism.

The abdominal wound was sutured and then, without much difficulty, the collapsed sac was removed and all the vessels from it ligated. It was, now, determined that the aneurism had its provenience in the sciatic artery. Rather troublesome was the tying off of the afferent sciatic artery, because the sac extended through the incisura ischiadica major into the pelvis. To facilitate the extirpation of the sac its posterior wall was split.[14]

The sciatic nerve was found to be so closely interwoven with the wall of the sac that it was thought to be necessary to remove about three-quarters of the circumference of this nerve.

On the following day, June 15, the patient's condition seemed to be satisfactory. The leg on the operated side felt warm, and its sensibility was preserved. No mention is made of pain in the limb.

June 16. p. m. Temperature 38.2°, pulse 142, and weak.

June 17. p. m. Temperature 38°, pulse 124. The left foot and leg felt cold, and sensation in them was lost. There were many deep, blue spots, irregular in outline and varying in size.

June 18. Patient became soporific. The blue spots were increased in size and number. Without the occurrence of other manifestations, the patient died at 11 p. m.

18. (Group II.) Körte, W. *Ligation of the right common iliac artery for ruptured aneurism of the external iliac. Consecutive ligation of the aorta. Death.* (Prof. W. Körte. Deutsche med. Wochenschrift, 1900, XXVI, 717.)

Male, æt. 28.

Anamnesis.—After an excessively wearisome journey in the mountains patient was seized with severe pains in the joints. Simultaneously there appeared nodules on the extremities which disappeared after taking iodide of potassium.

Early in March, 1899, patient observed a painless, pulsating swelling above the flexure of the groin. After a long bicycle ride on April 1, he experienced pain so severe that he was compelled to lie down. The right leg could not be used; the pains radiated down the front of the thigh, and acquired such intensity that he applied for admission to the Stadtisches Krankenhaus am Urban, Berlin, April 15, 1899.

Status.—A tall, lean, powerful, anemic man. Temperature 38, pulse 100-110, and easily compressible. The right limb somewhat œdematous and slightly flexed at the hip; cannot be voluntarily moved. Passive movements normal.

Above Poupart's ligament, on the right side, is a pulsating tumor the size of a large apple. The walls are tensely expanded. Distinct thrill and bruit over the tumor, and extending to the left to within about 4 cm. from the mid-line, and to the right to the outer edge of the right rectus muscle. Beyond these limits there is a resistant mass which entirely fills the right iliac fossa, extends upwards to the edge of the ribs and backwards to the long muscles of the spine. The pulsating tumor extends above to a point midway between navel and symphysis, and below to Poupart's ligament. Scarpa's triangle is filled out in such manner as to press forward the strongly pulsating femoral artery. Per rectum a thickening of the soft parts on the right pelvic wall is appreciable, and the pulsating tumor can be felt.

Compression of the aorta and of the right common iliac arrests the pulsation in the tumor. The heart is enlarged to the left. Over the aorta a diastolic murmur is to be heard and felt. Radial arteries tortuous. Urine free from albumen and sugar.

Diagnosis.—Aneurism of the right external iliac, ruptured; extensive extravasation of blood; aortic insufficiency and perhaps aneurism at the beginning of the aorta. Intraperitoneal ligation of the common iliac was determined upon. The extraperitoneal route was distinctly contraindicated because of the extravasated blood.

Operation.—April 17, 1899. Ligation of the common iliac with catgut. Pulsation in the aneurism thereupon ceased. For a few hours the right extremity was pale, but soon became warm and natural in color. Otherwise no disturbances of the circulation resulted from the ligation. In the femoral artery a slight pulsation was discernible. The toes could be moved; sensation remained unchanged. But for three days there were signs of intestinal paresis, nausea, singultus and tympany.

In the washing of the stomach, great quantities of dark fluid containing material resembling coffee-grounds were evacuated, and the first stools were blackish, as if blood-stained. It was concluded that the sub-peritoneal extravasation had either perforated the bowel at some point, or that it had compressed the mesenteric vessels (of the duodenum or ascending colon).

The sac of the aneurism remained pulseless and without bruit. The large hæmatoma on the right side did not, however, diminish in size and continued to cause distress.

On the second right intercostal space, alongside of the sternum, a pulsation, which could be seen and felt became manifest. Over this area systolic and diastolic murmurs were heard. On the 6th of May, and afterwards, there were signs of thrombosis of the femoral vein. The general condition of the patient did not improve; he remained pale, his pulse became more rapid, his temperature remaining normal, and he complained continually of pains in the hæmatoma, which radiated to the sacrum. The active movements of the right limb became more limited and, towards the middle of May the right leg was flexed at the hip. The hæmatoma in the right iliac fossa became very tense. Pulsation could not be perceived either in the aneurismal sac or in the extravasation, and was greatly diminished in force in the femoral artery. It was thought that the circulation in the

[14] It has, for many years, been a favorite procedure with surgeons to split, in two or in many parts, benign tumors otherwise difficult of removal. (*i. e.*, lipomata of the back of the neck.)

aneurism must have ceased, and that the perianeurismal hæmatoma had no direct communication with the blood stream. But as the patient remained unrelieved of his pain, it seemed indicated to open and empty the sac in the manner which had recently been recommended by Mikulicz.[15]

So 37 days after the first operation, on the 23d of May, 1899, a second was undertaken. The incision led into great masses of coagulated blood, which were extruded under great pressure. The tumor collapsed. As the cavity was almost completely emptied there took place, suddenly, a profuse arterial hemorrhage. This could, for a time only, be arrested by compression and tamponade. To search for the bleeding point in the enormous hole partly filled with coagula seemed unwise. Therefore, transperitoneally, through a mid-line incision, the aorta was ligated, at first over a little bunch of gauze. Thereupon the bleeding ceased. Then, through a long cut in the right flank, Prof. Körte completely evacuated the contents of the enormous cavity. At the right edge of the true pelvis, in the neighborhood of the internal iliac, he encountered a bright, but trivial hemorrhage which was controlled by pressure. The aortic ligature was now definitely tied and the wounds sutured. The patient was greatly collapsed, and died one hour after the operation.

At the autopsy it was determined that the patient suffered from widespread disease of the arterial system, which had led to the formation of aneurism of the aorta, right and external iliac, right femoral and right profunda femoris arteries.

19. (Group II.) Martin, A. A. *Ligation of the left common iliac artery for aneurism from a bullet wound of the external iliac. Recovery. Cure of aneurism.* By Arthur A. Martin, M. B., Ch. B. Edin., Civil Surgeon, South African Field Force. (Communicated by the Director-General, Army Medical Service. Brit. Med. Jour., Jan. 17, 1903.)

Private soldier, æt. 31. Admitted, Nov. 18, 1901, to General Hospital, Howick, Natal.

Examination.—Healed bullet wound of left groin. The wound of entrance was about three fingers' breadth above Poupart's ligament and internal to the external iliac artery. The wound of exit was below the crest of the ilium of the same side. The bullet had crossed the external iliac, "wounded the artery high up," and pierced the iliac bone. A marked bulging, expansive pulsation and bruit were noted, and the diagnosis of aneurism made.

Nov. 23. The aneurism, which had greatly increased in size, now extended a fingers' breadth below the umbilicus and to the middle line. The patient's temperature was 101.6° F.

Operation.—The incision began one and one-half inches above the center of Poupart's ligament, and extended to one inch above and internal to the anterior superior spine. The fascia and muscles were cut through in the line of the skin incision which, being found too short, was prolonged upwards in a curve with the convexity downwards and outwards. Peritoneum incised. The external iliac artery could not be defined. The common and internal iliac arteries seemed to enter the upper part of the aneurismal mass. The former artery, twice ligated, was divided between the ligatures of double silk. Wound undrained and sealed. The limb was enveloped in cotton wool and firmly bandaged.

Nov. 25. Patient said he could not "feel" his left leg.

Nov. 26. Vomited several times. No abdominal distension. The left leg was much colder than the right. "Roots of the toes very œdematous." Limb blanched. Skin below the knee quite anesthetic. No pulsation in tibial or popliteal.

Nov. 27. Large watery blebs on leg and foot. Anesthesia below the knee unchanged. No pain in groin since operation.

Nov. 30. Patient could "feel" his leg, which seemed "heavy as lead." Temperature of left leg nearly equal to that of the other side. Blisters and œdema vanished.

Dec. 22. The mass in iliac was smaller, hard and without pulsation.

Jan. —, 1902. Patient could easily flex, extend and rotate leg, but was unable to "lift it vertically" when lying on the back.

Feb. 3. Could walk about slowly. The mass in the left iliac fossa reduced to size of a goose egg.

The author makes the important comment that "the deep epigastric and deep circumflex iliac arteries fortunately came off below the aneurism."

20. (Group II.) Maynard, F. P. *Ligation of the right common iliac artery for diffused iliac aneurism. Death.* (The Indian Med. Gazette, Calcutta, 1903, p. 253. F. P. Maynard, F. R. C. S. (Eng.), Major I. M. S., Surgeon Superintendent, Mayo Native Hospital, Calcutta.)

Male, native, æt. 32. Admitted, April 17, 1903, to the Mayo Hospital.

History.—Patient had never had any venereal disease. Four or five months before admission he noticed a pulsating tumor in the right groin. Growing gradually larger, it did not pain him severely until a month later, when it began to increase rapidly in size.

April 7, after a stool, he felt "as if a gust of wind ran from his abdomen into the scrotum." Thereupon he noticed that the penis and scrotum had swelled, and experienced pain in these parts.

Status.—A tall, thin man with anxious expression. Pulse 99; respiration normal; temperature 100.8° F.; cough, but no physical signs of tuberculosis. Urine normal. A large, tense, rounded, pulsating tumor, occupying the right inguinal region, extended from about 2 inches below navel to 3 or 4 inches below Poupart's ligament. This swelling was continuous with the swollen scrotum, which also had expansile pulsation synchronous with the heart's systole. A loud systolic bruit, heard over the entire area of pulsation, was loudest at the upper and outer part of the tumefaction. The penis was very œdematous. The abdominal wall, as high as the left nipple, and the upper fourth of the left thigh showed a brownish discoloration from subcutaneous hemorrhage. Feeble pulsation could be felt in the right femoral and tibial arteries.

April 20. A portion of the scrotum had become black and anesthetic.

Operation.—An abdominal incision, in the mid-line, was carried below into the area of subcutaneous hemorrhage, where troublesome bleeding was encountered. The intestines gave great annoyance, and had to be brought out of the belly, where they were wrapped in warm, sterile towels. The operator regretted that he had not arranged for the Trendelenburg position. Three strands of silk were passed under the common iliac artery without difficulty. These were not drawn so tightly in tying as to cut through the inner arterial coats. Pulsation in the swelling ceased on tying the ligature.

April 21. Patient developed bronchitis and vomited occasionally.

April 22. Abdomen tympanitic. The aneurism was hard, the scrotum and toes warm. Bronchitis better.

April 24. Had several stools (diarrhœa), accompanied by the passage of some gas. The heat (106° F. in the shade) was very oppressive.

April 26. The diarrhœa and vomiting persisted. The aneurism had decreased in size. The wound seemed to be healed.

On the evening of the 27th, patient had several loose stools,

[15] Zur operativen Behandlungen der Aneurysmen. Beiträge zur klin. Chirurgie, Band XXIV, 5, 418. Hoffman.

and died quite suddenly. A post-mortem examination was not permitted.

The circulation of the extremity had not been manifestly affected by the operation.

21. (Group I.) Czerny, V. *Ligation of the left common iliac for the arrest of hemorrhage from a small branch of this artery torn from the parent-stem in the course of operation for the removal of tuberculous glands.* (Dreist. Deutsche Zeitschrift f. Chirurgie, 1904, p. 10.)

Male, æt. 28. Admitted to the surgical clinic for pelvic tumor. Had four years previously been admitted to the hospital for traumatic hæmarthrosis genu and hæmatoma femoris.

Examination.—The tumor in the pelvis, although quite hard, gave evidence of fluctuation. It was movable on the ilium. Per rectum there was felt, in the neighborhood of the symphysis sacroiliaca dextra, a resistent body lying upon the bone, which it was thought might be an exudate.

Diagnosis.—Lymph glands, suppurating, and probably tuberculous.

Operation.—Feb. 26, 1897, by Prof. Czerny. Nodular masses composed of glands were, without much difficulty removed from along the inner edge of the ilio-psoas muscle, but not so easily from the external iliac artery, which for 5 cm. was imbedded in them, mesially. In separating the packet of glands from the vessels, a small branch of the common iliac artery was torn off so near its parent stem that ligation of the latter, being considered imperative, was done. Three ligatures of thick catgut were employed, but not drawn so tight as to cut through the arterial wall. Other conglomerations were found, *i. e.*, in the pelvis and præsacral area. The removal of the diseased glands was continued without other untoward incident. It was constated that the deep epigastric vessels were not injured. The wound was tamponed.

During the first two days the left extremity was somewhat cold. There was no disturbance of sensation following the operation, nor was there any pain.

On and after the 10th of March, there were irregular elevations of temperature, at first associated with frontal headaches. Pulmonic râles were detected; then followed night sweats and slight expectoration, and on the 30th of July, 1897, the patient died of acute miliary tuberculosis.

At autopsy a double ligature was found on the common iliac artery, with associated thrombus extending to the bifurcation of the aorta. The collateral circulation seemed to have been established largely by means of anastomosis between the internal iliac arteries of the two sides without the presence of any large communicating branch.

22. Kuster, Ernst. *Ligation of the left common iliac and other arteries for elephantiasis of the lower extremities. Result negative.* (Karl Dreist, Deutsche Zeitschrift fur Chirurgie, 1904, LXXI, 32.)

Female, æt. 17. Admitted, Dec. 3, 1897, to the surgical clinic of the University of Marburg.

Anamnesis.—Parents and five brothers and sisters alive and well. Two years ago, just after illness with nettle-rash, both legs became swollen, but without causing any discomfort. The swelling has steadily increased. Menstruation began in her 16th year and has always been irregular.

Status on Admission.—Body well nourished. Skin rather pale. Findings in thorax and abdomen normal. Pulse slow and somewhat irregular. Urine normal. Both lower extremities large and shapeless. Thighs 54 cm. in circumference. The left calf 45 cm. The feet are uninvolved. The skin feels abnormally solid; its veins here and there are dilated. There are telangiectases on the chest, left arm, forearm and hand.

Treatment.—Elevation of the limbs and compression.

Dec. 8. The swelling of the thighs is diminished by 6 cm.; of the legs by 5 cm.

Dec. 20, a. m. Allowed to stand for the first time; p. m., the legs are again as large as ever.

Jan. 7, 1898. *Ligation of the right femoral artery below Poupart's ligament.* The subcutaneous fat was so thick that the finding of the artery was very difficult. The limb became paler after the operation.

Jan. 18. Decided decrease in the circumference of the right extremity. The skin has become softer.

Jan. 28. *Ligation of the left femoral artery below Poupart's ligament.*

Feb. 10. Reduction in size of the left limb.

Feb. 25. Patient being permitted to stand, the swelling promptly increased.

March 8. *Extraperitoneal ligation of the right external iliac.* The vessel was very small. Tamponade. Erysipelas.

April 24. Extremities normal in size.

April 30. Patient allowed to walk. No swelling observable in the evening.

May 12. Swelling as great as on admission.

June 23. *Extraperitoneal ligation of the left common iliac.* Limb cooler towards evening.

June 27. Temperature of both extremities the same.

Aug. 2. Result of the operations negative.

23. (Group I.) Trendelenburg, Friedrich. *Ligation of the left common artery for aneurisma dissecans of this vessel. Death.* (Communicated by Dreist, l. c., p. 12.)

Male, æt. 60. Admitted, Oct. 4, 1898, to Prof. Trendelenburg's clinic in Leipzig.

Examination.—General condition wretched. Patient had suffered from pain in the abdomen for a year, and on the day of admission had done a full day's work, although repeatedly complaining to his fellow laborers of drawing pains. Suddenly, about 6 p. m., very severe pains set in, and he rapidly became pale and weak.

Status on Admission.—Patient very pale and in great pain. There was eructation but no vomiting. The abdomen was greatly distended. Liver dullness normal. On the left side of the abdomen was palpated a tense, elongated tumor of the size of one's arm, which, in its course, corresponded to the situation of the descending colon. The percussion note, nowhere metallic, was dull over the tumor. Nevertheless it was thought that perhaps there was volvulus of the sigmoid flexure, and an exploratory laparotomy was promptly made.

On incision of the abdominal wall, a large amount of blood was observed extravasated in the præperitoneal space. The hand in the abdominal cavity ascertained that the tumor was retroperitoneal.

An incision was made into this hæmatoma. On removal of coagula there was, at first, no fresh bleeding, and there was found at the bottom of the large cavity a pulsating aneurism with rounded surface, which led towards the aorta, but was situated between the lumbar vertebræ and the psoas muscle. Suddenly there spurted from the aneurism a thick stream of blood. Compression was made; but under the compressing finger the rent in the aneurism became greater, whereupon the blood welled forth in a great flood.

The aneurism was laid freely open, and a ligature applied to its root, near the aorta. Hemorrhage from the distal side was controlled by a clamp and by tying off the rent with a strip of gauze. Skin suture. Infusion of 900 cc. salt solution. Patient awoke from the narcosis, evinced great restlessness, and died in three hours.

Autopsy.—Dissecting aneurism of the right common iliac. Fusiform aneurism of the left common iliac, the size of a hen's egg, immediately below the aortic bifurcation. A tear of the intima, in the middle of the aneurism, transverse to its long axis. Diffuse arteriosclerosis of the entire aorta. Arteriosclerosis with calcareous infiltration of the right coronary artery of the heart and of both iliacs.

24. (Group II.) Christel. *Ligation of the left common iliac artery for spurious aneurism of the femoral. Recovery. Gangrene.* (Dreist, l. c., p. 6.)

Male, æt, 28. Blacksmith. On Jan. 28, 1901, a glowing splinter of iron penetrated the left thigh, and thereupon a strong pulsating stream of blood spurted from the wound. Patient controlled the bleeding with his thumb until the arrival of a physician, who applied a compressing bandage. Eight days after the injury, patient was allowed to go about. Severe pains, with tension in Scarpa's triangle, compelled him to take to his bed again. The swelling increased and the pains became unbearable.

March 1, 1901. Admitted to Rombacher Spital, Metz.

Status.—March 5. Patient was greatly emaciated and anemic. Resembled a consumptive in the last stages of the disease. Pulse, thready (126+). Rectal temperature 36.7°. Left thigh enormously swollen. A small scar, 10 cm. below anterior superior spine, along the inner edge of the sartorius. The œdema extended to the level of the navel. Skin of the thigh livid, and its veins distended in the region of the tumor. Auscultation over it negative. Pulsation in the posterior tibial artery was distinct.

Diagnosis.—Spurious aneurism, with beginning suppuration of the femoral or a branch of this artery.

Operation.—March 6. Incision over the greatest convexity of the tumor led into a large hole, between the extensor and adductor muscles, lined with coagula. The femoral vein was thick as a finger, tensely full and non-pulsating. Blood welled up from the depths of the wound. Attempts to remove the clots from the infiltrated and friable tissues caused such very profuse bleeding that they were abandoned. Preparations made for the ligation of the external iliac. An incision parallel to Poupart's ligament laid bare this artery, which was then ligated below the origin of the deep epigastric, because the latter vessel was given off at an abnormally high point. During the manipulations, the epigastric was torn off and ligated. The external iliac was again ligated above the origin of the epigastric.

Then the wound of the thigh, which had been tamponed with gauze, was reinvestigated. There was still bleeding from several unrecognizable sources. The patient was so collapsed that a further loss of blood could not be sustained. Hence it was determined to ligate the common iliac. This was done extraperitoneally. The bleeding from the wound of the thigh was thereby arrested. The femoral artery was again searched for in this wound but not found. Both wounds were tamponed with iodoform-gauze.

"After a time," the left leg became cold and insensible. A livid discoloration of the foot appeared. The gangrene extended gradually. A line of demarcation formed about the junction of the middle and upper thirds of the leg. The patient became soporific. Pulse 124; temperature 103.5° F. Notwithstanding the desperate condition of the patient, Dr. Christel amputated "the same day." Gradual recovery took place, and Oct. 6, 1901, the patient was supplied with a prothesis.

In March, 1903, Dr. Dreist again saw the patient, who had entirely regained his health.

Whether it was the femoral, or a branch of this artery, which had been injured by the iron splinter, was never determined. What vessels besides those mentioned may have been ligated or injured is not known. It is at least certain that the gangrene is not to be attributed solely to the ligation of the common iliac. Inasmuch as the external iliac was ligated above and below the torn off epigastric artery, it is probable that the circumflex iliac also had its origin between these ligatures. The profunda femoris with its circumflex branches may have been injured either by the iron splinter or in the attempts to check the hemorrhage from the wound of the thigh.

25. (Group I.) Clark, Henry E., C. M. G. Senior Surgeon, Glasgow Royal Infirmary. *Ligation of the left profunda femoral and common iliac arteries for wound of the profunda artery and vein. Recovery.* (Brit. Med. Jour., Oct. 7, 1905, p. 850.)

This case is so briefly and picturesquely reported that I retell the story in the words of the operator.

"H. B. Porter, aged 26, was admitted into Ward 25, Glasgow Royal Infirmary, on April 25, 1899, suffering from a small punctured wound at the inner side of the left thigh, at the junction of the upper and middle third.

"His story was that he and another man were having a fight, when the latter whipped out a penknife and came at him. In trying to escape from the assault, he fell, and his assailant fell on top of him, and the blade of the knife ran into the thigh, right up to the hilt. The wound bled very freely, but a doctor was soon in attendance, who put on a pad and a bandage. When he reached the hospital the bleeding had ceased, and on the following morning, when I saw him at the usual visit hour, the wound was so well plugged with clot that I thought it unwise to disturb it. All went well till May 12, when the wound was found to be bleeding freely, suppuration having taken place, and the clot having consequently broken down. I thoroughly opened up the wound, and exposed the main trunk of the profunda femoris artery, which had been incompletely divided; this was double ligatured and cut across. The vein was also found to be injured, and was more difficult to secure effectively than the artery.

"Three days afterwards (on May 15), when the patient was using the bedpan, he became suddenly blanched and pulseless, and the dressings became saturated with arterial blood. I was fortunately on the spot at the time, and at once took him to the operating theater, where I ligatured the common femoral artery just at its emergence from beneath Poupart's ligament. This arrested the bleeding, and he very rapidly recovered from the loss of blood, until five days later (May 20), when a still more serious hemorrhage took place. On this occasion, also, I happened to be in the infirmary and at once applied an elastic bandage round the pelvis and hip, but as this did not control the bleeding, it was decided to ligature the common iliac artery. This was done by Sir Philip Crampton's method, as described by him in the Medico-Chirurgical Transactions, Vol. XVI, p. 161, as far back as 1828. The incision commenced at the anterior extremity of the last rib, proceeded downwards directly to the ilium, then followed the line of the crest, but keeping a little within its inner margin, until it terminated at the anterior superior spine. The abdominal muscles were divided in the full extent of this incision till the peritoneum was reached, when that structure with the contained intestines was lifted up off the iliac and the lumbar fasciæ. The ureter was raised with the peritoneum. An excellent view of the external and common iliac arteries was obtained, and the bleeding was slight and easily controlled. By means of a helix-curve aneurism needle the common iliac artery was freed from a small amount of fat, and a strong chromic gut ligature passed and securely tied. The large wound was for the most part stitched up in layers, but the part in the loin was packed with iodoform gauze. The patient stood the operation well, and made up rapidly for the loss of blood. Unfortunately, the wound suppurated, but this was not wonderful, considering that there had been all along an infection of the original wound, probably from septic material carried in by the knife. This, however, materially delayed the healing,

and it was not till August 11 that he was dismissed to the Convalescent Home.

"After leaving the wards he was only seen once by me, as he found it impossible to come to the infirmary on week-days. He was seen by one of my dressers, and also by my staff-nurse fully six months after leaving us, and was then in full employment as an outside porter at the Glasgow Central Railway Station. I understood his work to consist mainly in taking commercial travellers' large sample boxes on a hand-barrow about the town—a sufficiently trying and laborious occupation. It is not too much, I think, to claim this not only as a 'recovery' but as a perfect cure."

26. (Group II.) Cranwell, D. I. *Ligation of the right common iliac for aneurism of the external iliac and femoral arteries. Gangrene. Death.* (Tratamiento de los anuerismos de la iliaca externa. Por el doctor Daniel J. Cranwell, Profesor suplente de clinica quirurgica. Revista de la Sociedad Médica Argentina, 1906, Vol. XIV, p. 388.)

Male, æt. 48. Blenorrhagia at the age of 16 years. Alcoholic. Thirty years ago, after a walk, he suffered with cramps in the right leg which made him halt. Later, a small tumor appeared in the right groin which for 15 years grew slowly, and then more rapidly, until August, 1903, when he received a blow in the affected regions. Ever since then the growth has increased and the leg has been swelling. For the past 30 years he has had intermittent pains in the lower part of the thigh at the base of Scarpa's triangle and in the knee, which were greater at night and with exercise.

Status.—A very lean individual in bad general condition. The thigh is flexed, abducted and rotated outwards. Occupying the base of Scarpa's triangle and the right iliac fossa, there is a tumor as large as the head of a child. Poupart's ligament indents the mass, the lower part of which, as big as an orange, is somewhat drawn out in the course of the femoral vessels. The skin over it is normal, and not adherent to the underlying tumor. The swelling is soft and expands with pulsation. The thigh and leg are œdematous. Patient suffers excruciating pain in the hip and inner part of the thigh. Motions of the joint are greatly restricted because of the pain. He has numerous subcutaneous lipomata and general arteriosclerosis.

Diagnosis.—Aneurism of the external iliac and femoral arteries.

Operation.—Feb. 28, 1904 (?). Trendelenburg position, median incision. Transperitoneal ligation of the right common iliac just below the bifurcation of the aorta. Immediate cessation of pulsation in the aneurism.

March 1. The leg was livid and without sensation from the calf to the toes.

March 2. Gangrene of the leg. Amputation about the middle of the thigh.

The patient's general condition improved for a time, but the wound showed no tendency to heal. The arteries were rigid and pulsated forcefully.

April 4. Sacral decubitus. Death.

27. (Group II.) Gillette, Wm. D. *Ligation of the left common iliac artery for the cure of ischiadic aneurism. The internal and external iliacs were also ligated and the sac dissected out and tied off. Gangrene.* (Annals of Surgery, 1908, XXXVIII, 22.)

Patient, male, æt. 56. Aneurism of left sciatic artery attributed to severe fall about 17 months prior to operation. The aneurism extended so high towards the pelvis that ligation of the afferent artery was not attempted. So (April 22, 1905) the left internal iliac was tied near its origin. The patient recovered uneventfully. Pulsation ceased in the aneurism, which rapidly diminished in size. For seven months a cure was believed to have been effected. Then pulsation reappeared in a small tumor at the original site of the aneurism. Patient did not consent to further operation until three months later, when the aneurism had greatly enlarged, although not to its former dimensions, April 18, 1906. Dr. Gillette exposed the pulsating tumor in the buttock, hoping to ligate the artery leading to it, or to perform the Matas operation. Neither procedure was feasible. The abdomen was then opened and, as compression of the external iliac artery seemed to obliterate the pulsation in the aneurism, this artery was ligated. But on re-examination of the tumor, it was found that the pulsation had not been affected in the least. So the common iliac artery was tied close to the aortic bifurcation. Then, through the incision in the buttock, the sac of the aneurism was freely opened and tied off at the highest possible point.

On the third day signs of gangrene of the leg appeared, and on the sixth day amputation was made at the juncture of the upper and middle thirds of the leg. Sloughing of the flaps necessitated amputation of the thigh. Recovery.

28. (Group II.) Halsted, W. S. *Occlusion of the left common iliac with an aluminum band for aneurism of the external iliac and femoral arteries. Recovery. Aneurism cured.* (*Case hitherto unreported.*)

M. R., German, æt. 44, was admitted to the Johns Hopkins Hospital December 28, 1908, complaining of tumefaction and pain in the left groin.

Story.—Has always enjoyed good health. Believes that he had malaria at some time. Contracted specific urethritis at the age of 22, and at the same time a venereal sore which was accompanied by enlarged inguinal glands. Has had no secondary manifestations of lues. Drinks two bottles of beer daily, is otherwise temperate. About two and one-fourth years ago, patient in falling, was struck in the left groin with the iron-bound edge of a barrel. He suffered no immediate inconvenience from the trauma, but three months later felt a "drawing" pain in the left groin and leg. This pain was especially severe in the calf, and prevented him from doing much walking.

Four or five months after the injury, the leg began to swell. About September, 1908, the pain ceased, in the leg, but increased in the groin, where it assumed a "burning character." More than one and a half years ago a lump in the groin was noticed. This has been "getting larger" and tender, and patient has observed that it pulsates. The burning pains in the swelling are intensified by walking.

Status præsens.—Patient is well nourished and seems to be robust. Examination of the eyes, ears, nose, mouth, chest and rectum reveals nothing abnormal. Radial and temporal arteries slightly hard and tortuous. Pulse 90. Cicatrices in both groins. In the left groin is a large, very tense pulsating mass, over which the skin, œdematous, reddish and glistening, is tightly stretched. The swelling extends laterally to the anterior superior spine of the ilium, mesially to the mid-line, upwards to within 8 cm. of the umbilicus and downwards to a point 12 cm. below Poupart's ligament. It measures 26 cm. in the transverse, and 20 cm. in the longitudinal diameter. It has forced the external ring downwards and the canal forwards, so that the finger cannot enter the former. The mass expands in all directions with the pulsation, the heave from which is so strong that motion is communicated to the penis and scrotum with each heart-beat. A loud systolic bruit is to be heard, and a thrill to be felt, over the tumor.

The right foot is colder than the left. Pulsation in the popliteal, posterior tibial and dorsalis pedis arteries is not perceivable. The left thigh at 20 cm. above the patella measures 51.5 cm., the right 47 cm.; the left calf 35 cm. the right 30.5 cm. The veins and venules of the left limb are enlarged. Sensation and motility are normal. White blood corpuscles 8400. Hæmoglobin 81 per cent (Sahli).

There seems to be a delay of pulsation in the tumor of three hundredths of a second. The lower edge of the swelling is abrupt, and a little overhanging. The patient rests most comfortably with the thigh slightly flexed and abducted. There is an apparent lengthening of 3 cm. of the left lower extremity.

The temperature was usually 0.5 of a degree (Fahr.) higher in the left than in the right popliteal space.

Diagnosis.—Aneurism of the external iliac and femoral arteries.

Operation.—Jan. 11, 1909. Application of a totally occluding aluminum band to the left common iliac artery. The patient was placed in the Trendelenburg position to compel gravitation of the intestines towards the thorax.[16] A vertical incision was made through the middle of the anterior sheath of the rectus muscle. This muscle was then split near its inner edge, and its external portion retracted outwards. The posterior sheath of this muscle, the fascia tranversalis and the peritoneum were divided about in the line of the incision through the anterior sheath and skin.

It was my intention to ligate the external iliac artery if possible. The upper side of the huge aneurism presented a vertical face which seemed to be almost flat, and the external iliac artery lay at a great depth behind the aneurism. A very thick panniculus considerably increased the distance of the artery from the skin. The vertical diameter of the aneurism at its upper edge was estimated at 12 cm. to 13 cm. We possessed no retractors which could reach to the bottom of the wound, but by means of broad spatulæ and the hand of an assistant, the intestines, which had been carefully displaced upwards and to the right side, were kept easily out of the way.

The left ureter promptly came into view, and beneath it the common iliac artery was recognized. This was readily isolated by means of two long fine blunt dissectors, designed especially for the dissection of the deep arteries (*i. e.*, the inferior thyroid). The left common iliac being raised from its bed by two narrow tapes, an armed band roller was passed under it in the usual manner,[17] and the band (6 cm. wide) curled by the instrument. On releasing the traction-pressure made on the artery by the tapes, the expanded vessel not only completely filled the band, but was constricted by it. A very slight additional rolling of the band with the fingers sufficed to arrest the pulsation in the aneurism, but not altogether in the common iliac artery.

The thrill, however, which is observed with a certain amount of partial occlusion of an artery had vanished. A little additional rolling of the band—so little that I was not able to appreciate with the fingers that a further constriction had been accomplished—shut the pulse off completely from the artery, which assumed a flattish shape and the almost collapsed appearance characteristic of empty arteries. The peritoneum, transversalis fascia and posterior sheath of the rectus were closed with a continuous catgut suture, and the anterior sheath of this muscle in the same manner. The subcutaneous fascia was stitched with interrupted sutures of very fine silver wire. A continuous buried mattress suture of strong silver wire was employed for the skin, because considerable traction was necessary to bring its slightly inflamed edges together over the tumor. Under such conditions catgut is useless, and silk would prove a nuisance should suppuration occur. Where there is tension of the skin, the buried silver wire suture has proved, in our experience, to be the best. The wound was covered with silver foil.

Returned to the ward at 1.45 p. m., the patient's pulse was 100, his temperature 97° F. There was no return of pulsation in the aneurism. During the afternoon he was restless and complained of pain in the left leg. The left foot seemed cooler than the right, but was of good color, though the circulation was somewhat impeded. There was no impairment of motion or sensation.

3.20 p. m. The temperature in the popliteal space is 97.4° F. on the left, 97.3° F. on the right side. At 6 p. m. the temperature of the feet is relatively the same on both sides as at 3.20 p. m., but in the popliteal space, and for a short distance down the leg, it is a few tenths of a degree higher on the left than on the other side.

Until midnight the color of the foot remained apparently unchanged. Then there seemed to be a slightly bluish tinge of the skin of the left foot, which remained for not more than two hours. At no time did the patient observe any unusual sensations in the foot, but he complained of excruciating pain in the left leg between the knee and ankle, and in no other place. Something seemed to be "bearing down on the bone, hard enough to break it." Over a small area, about 3 cm. in width, on the inner side of the calf of the left leg, the touch of the finger could not be appreciated.

Jan. 12, 8 a. m. The patient's condition is highly satisfactory. The pain in the leg which persisted during the night has almost vanished. The circulation in the left foot is improved. Temperature in popliteal space 96.8° F. on the left, 96.4° F. on the right side.

9 p. m. The swelling in the limb is diminishing; the measurements showing 2.5 cm. decrease in size at 10 cm. and 20 cm. above the patella.

Jan. 13. Patient passed a comfortable night, with very little pain in the leg. The foot has remained warm and its color good. There is little distension of the abdomen. At 8 a. m., temperature 99.4° F., pulse 120, respiration 20. There is no perceptible pulsation in the aneurism or in the arteries below. The tumor seems to be softer.

8 p. m. Temperature in popliteal space, right 98.2° F., left 98° F.

Jan. 14. Abdominal distension entirely relieved.

Jan. 15. Aneurismal mass seems flatter and softer. There is no observable pulsation.

Jan. 17. *First dressing.* The tense skin is reddened along the greater part of incision, about the middle of which there is a gaping of nearly 4 cm. Patient says, "I have never felt better in my life."

Jan. 20. The redness of the skin has about disappeared. There has been no further separation of the edges of the wound, the exudate from which is still serous. The swelling of the leg continues to decrease. No pulsation in the aneurism or arteries of the extremity.

Jan. 31. Aneurismal mass measures 13.5 cm. by 15.5 cm. Apparent lengthening of left leg is still 2 cm. (abduction).

Feb. 8. Patient has been up in a chair for the past three days. There has been no swelling of the leg incident to its dependent posture. No pulsation in the tumor. The wound is healed.

Feb. 10. Patient walks without difficulty or discomfort. There is no swelling of the foot.

Feb. 12. Slight pain in calf, relieved by massage. Left foot and leg slightly cyanosed.

Feb. 15, 1909. Sensation of entire leg normal, but at the inner side of the thigh, just below the groin, there is an area about 9 cm. long over which the patient is unable to distinguish heat and cold accurately, or to appreciate the difference between the lightly applied point and the head of a pin. The tumor mass is smaller, harder, more sharply circumscribed, and without pulsation. Patient discharged.

Jan. 19, 1910, *one year after the operation.* Patient writes: "I am getting along splendidly, and the aneurism has completely left me. I sometimes experience a little pain in my left leg when walking fast, otherwise can complain of nothing. Am very fat, my weight being 180 pounds."

A photograph of the groin, received a few weeks later, shows no trace of the aneurism, only a broad vertical scar.

[16] In operations upon the aorta of dogs this posture was found to be of great service.

[17] Journal of Experimental Medicine, 1909, Vol. XI, 373.

April 4, 1912, *three and a quarter years after the operation.* Patient writes: "In reply to your letter of the first, I will try to explain how I am feeling. My left leg is a great deal weaker than my right. I don't limp any. I can't walk very much, as I have pains in my left leg when I do any walking, and in case it gets very cold. My present weight is 180 pounds. I have a splendid appetite, and haven't been ill since my return. All traces of the aneurism have disappeared, and it never worries me the least bit."

29. (Group II.) Beckman, E. H. *Partial occlusion by the Neff clamp*[18] *of the left common iliac artery, presumably for arterio-venous fistula of the femoral artery and vein.* (Communicated to me by Dr. E. H. Beckman, Mayo Clinic, Rochester, Minn., March 6, 1912.)

Dr. Beckman's letter is as follows:

"Patient was a male, 27 years of age, who had been operated upon 11 years previously for osteomyelitis at the lower end of the left femur. The surgeon told him that the artery had been injured at the time of operation. He noticed a marked thrill in the femoral artery. The osteomyelitis wound healed and has given him no further trouble. Patient has had a marked thrill and increased pulsation along the entire femoral artery, and extending above Poupart's ligament, from the time of his operation, but he has been able to continue at work as a paperhanger. He consulted us because, for the past three months, he had had increased pain and tenderness along the course of the femoral artery. We found, upon operative examination, that the femoral artery was dilated to about the size of an aorta throughout its entire length, the dilatation extending above Poupart's ligament. At our *second operation*, performed 11 days after the first, we made an abdominal incision and found that the left common iliac artery looked like the extension of the aorta, being dilated to the same size as the abdominal aorta. The right common iliac artery looked like a small branch coming from the main vessel.

"A Neff clamp was applied to the common iliac artery just below the bifurcation of the aorta, tight enough to partially occlude the former vessel, but not so tight as to arrest the pulsation in the right femoral artery.

"It was thought that the patient also had a small tuberculous abscess at the site of the old osteomyelitis. This presented in the scar of his original operative wound about a week following our first operation and was drained. The patient had several chills, and ran a high temperature for 24 hours following these chills, but otherwise made a good recovery.

"It has now been two months since the clamp was applied, and the patient feels that he is very much improved. He has returned home and will report to us from time to time."

30. (Group II.) Judd, Edward S. *Partial occlusion by the Neff clamp of the right common iliac artery for aneurism of the external iliac. Death.* (Communicated to me by Dr. Edw. S. Judd and Dr. B. F. McGrath, Mayo Clinic, Rochester, Minn., March 25, 1912.) Dr. Judd's letter is as follows:

"Case 61582. Male æt. 28. Examined at the Mayo Clinic, November 27, 1911.

"*Previous History.*—Ten years ago, pneumonia. Six years ago, operation for right inguinal hernia.

"*Subjective Symptoms.*—For the past year the patient has felt a throbbing sensation in the right side of the abdomen, about two inches above the hernial wound. Three weeks ago, and occasionally since then, he has suffered from sharp pleuritic-like pains in the same region on lifting. Otherwise feels well.

"*Objective Signs.*—There is a pulsating mass in the lower abdomen, slightly to the right side. A bruit is heard over the mass. Pulsation of both femoral arteries is absent. The mass pushes into the anterior wall of the rectum, low down. The inguinal glands of both sides are enlarged. The right leg is somewhat swollen. The lower abdominal veins are prominent. A scar resulting from the operation for right inguinal hernia is present. X-ray negative; Wassermann, negative.

"Admitted to St. Mary's Hospital, Dec. 6, 1911, for observation. Temperature and pulse normal to time of operation.

"*Operation.*—Dec. 29, 1911. A low abdominal exploratory incision was made to the left of the mid-line. An aneurismal sac occupied nearly the entire pelvis and bulged over the pelvic brim, thereby obscuring its exact origin, but affording the observation that it arose from the right side of the pelvis.

"A long oblique incision was then made in the right loin, exposing, but not opening, the peritoneum. The latter was reflected, the aorta exposed and the right common iliac artery reached by the guidance of the pulsating wall of the aneurismal sac. The right ureter and the right common iliac vein were isolated, pushed aside, and a Neff occlusion-clamp applied to the common iliac artery about one inch above the aneurism. The clamp was then gradually closed until but a faint pulsation of the tumor was noted.

"*Post-operative Course.*—The pulse was 130 for several hours after the operation, and then varied between this and 162 until the end. Vomiting for the first 24 hours. Severe pain in the right leg. Pulsation of femorals absent. Color of right leg good for two days. Died, Jan. 1, 1912.

"*Autopsy.*—(B. F. McGrath.) An incision to the left of the mid-line, 15 cm. long, is firmly closed with suture. This region is bulging, and there is some ecchymosis about the suture line. In the depth of the same incision is a considerable number of clots, apparently the result of venous oozing. On the right side is a closed oblique incision about 19 cm. long, passing in front of the anterior superior spine of the ilium; this incision extends to, but not through, the peritoneum. The right, lower extremity is very much swollen. On the inner side of the thigh there is venous thrombosis.

"*Thorax.*—Lungs and pleural cavities, nothing noteworthy. The heart is somewhat enlarged, otherwise it presents no changes.

"*Abdomen.*—Liver, moderate degeneration. Kidneys, considerable acute nephritis. A tumor extends from the umbilicus to the left side of the pelvis and down to the right groin. A Neff occlusion-clamp is in position on the right common iliac artery 3 or 4 cm. from the bifurcation of the aorta. About 2.5 cm. below the clamp the artery passes into the tumor, which proves to be an aneurism of the right iliac, its inferior extremity extending to about the beginning of the femoral artery. The left pelvic portion of the tumor consists of a fist-sized fatty mass, rather lightly attached to the aneurismal sac. The aneurism contains dark clotted blood, which is partially organized, and somewhat occludes the lumen.

"Within the artery and directly beneath the aneurism is a valve-like projection from the posterior wall of the vessel. The lateral and anterior edges of the projection are thin and unattached, but in contact with the vascular wall. Its upper surface is somewhat concave, and receives the lower end of the organized blood clot. Its structure is of nearly cartilaginous consistency, and the neighboring lining of the vessel is roughened and firm; sections from this area show principally dense fibrous tissue.

"At the autopsy nothing was found to account for the patient's death. The operation was an extremely difficult one, and required considerable time, and while the patient reacted fairly well, the reaction was not complete. I think there is no possible chance that the clamp could, even partially, have occluded the aorta."

In the opinion of Dr. Judd the operation for hernia, six years ago, was responsible for the aneurism.

[18] Journ. Amer. Med. Asso., 1911, LVII, 700.

TABLE A.—LIGATION OF THE COMMON ILIAC ARTERY.—CASES REPORTED SINCE 1880.

No.	Group.	Operator.	Published.	Date of Operation.	Complications.	Mortality.	Gangrene.	Indication.	Comments.
1	I	O'Grady.	Med. Press and Circular, 1880.	1877, Nov.	Arterio-venous fistula; infection; hemorrage; ligation of femoral and internal iliac arteries.	+	—	Arterio-venous aneurism of the femoral vessels.	Enormously enlarged femoral and external iliac arteries, the latter "resembling a coil of intestine." Death from hemorrhage.
2	II	Richter.	Pacific Med. and Surg. Report, 1880-1.	1881, Feb.	Gangrene before operation.	—	+	Aneurism of external iliac.	Observed only one month after operation.
3	II	Nicoladoni.	Wien. med. Presse, 1882, Nos. 7, 8, and 9 (Aug. Sulzenbacher).	1881, Feb.	Hemorrhage; ligation of external iliac, epigastric and femoral arteries; thrombosis of wounded femoral vein.	+	—	Spurious aneurism of hypogastric and iliac regions.	Spurious aneurism of inguinal region. No reference is made to the circulation of the foot. Death from hemorrhage and prolonged operation (3½ hours) under profound narcosis (chloroform).
4	II	Lange.	New York Med. Jour., 1883.	1883, July.	.....	—	+	Illo-femoral aneurism.	"Small cutaneous necrosis of the great toe."
5	I	Kümmel.	Verhandl. der deutsch. Gesellsch f. Chir., 1883.	1883, Nov.	Ligation of ext. iliac (twice), femoral (3 times), and finally of the profunda and circumflex arteries.	—	+	Arrest of hemorrhage.	The circulation of the limb remained good until, finally, the ligation of the profunda and circumflex arteries was made. Amputation.
6	II	Schönborn.	Centralblatt f. Chirurgie, 1884 (Stetter).	1883, May.	Infection.	—	+	Aneurism of internal and external iliac arteries.	Gangrene confined to highly infected wound and its neighborhood. No return of pulsation in the aneurism of the internal and external iliac arteries. "Cure." Observed only 6 months.
7	I	Kümmel.	Arch. f. klin. Chir. 1884.	1883, Dec.	Multiple aneurisms; exhausting hemorrhages; gangrene preoperative; ligation of ext. iliac artery.	+	+	Arrest of hemorrhage; multiple aneurisms.	Common iliac ligated to control hemorrhage from ruptured aneurism of calf after lig. of ext. iliac had failed to do so. Interesting to note that lig. of the ext. iliac arrested pulsation in the femoral aneur. for only 2 hrs.
8	I	Gouley.	New York Med. Jour., 1885.	1871, Oct.	Pyæmia.	+	+	Diffuse aneurism of the external iliac.	Circulation in limb not manifestly disturbed and no pain in foot or leg until 18th day. 19th day echymoses about ankle and intense pain in leg.
9	II	Jameson.	Lancet, Lond., 1886.	1885, Apr.	.....	—	—	Aneurism of external iliac.	Aneurism of the right ext. iliac, so large that ligation had to be made through a left-sided incision. "Cure." Observed only 6 months.
10	II	Fluhrer.	New York Med. Record, 1886.	1886, May.	Aneurism of the abdominal aorta; nephritis.	+	—	Aneurism of external iliac.	Death from nephritis.
11	II	Smith.	Trans. Clin. Soc., Lond., 1887.	1885, Oct.	Peritonitis (?); thrombosis of ext. iliac, fem. and profunda veins and of int. iliac, fem. and profunda arteries.	+	+	Ilio-femoral aneurism.	Amputation for gangrene, signs of which appeared in 24 hrs.
12	II	Lucas.	Brit. Med. Jour., 1892 (W. Mitchell Banks).	1888.	.....	—	—	Aneurism of external iliac.	Report incomplete.
13	I	Meyer.	Annals of Surgery, Phila., 1894.	1893, Oct.	Lig. of both of the internal iliac and of external iliac arteries; hemorrhage; infection.	—	+	Secondary hemorrhage.	"Partial gangrene of toes."
14	II	Stevenson.	Lancet, Lond., 1896.	1895, Nov.	.....	—	—	Diffuse aneurism of external iliac and femoral arteries.	For two weeks spontaneous cure of the ilio-femoral aneurism seemed to have taken place. "Cure." Subsequent history not given.
15	II	McBurney.	Annals of Surgery, Phila., 1898.	1897, Dec.	.....	—	—	Aneurism of external iliac.	The aneurism terminated below at Poupart's ligament. At no time were there signs of impairment of circulation. Pains in the leg not mentioned. Brief report. "Cure." Observed only 3 months.
16	II	Bryant.	Annals of Surgery, Phila., 1898.	1893 (?)	.....	+		Aneurism of external iliac.	Cause of death not given. Gangrene not mentioned in the very brief report.
17	II	v. Büngner.	Dissertation, Marburg, 1899, v. Varendorff.	1898, June.	Hemorrhage; excision of sac of the aneurism (ischiadic); aneurism of internal iliac; mitral insufficiency; general arterio-sclerosis; old age (66 years).	+	+	Aneurism of the sciatic and external iliac arteries.	Operation of Philagrius (tying all vessels leading to sac) attempted prior to and completed after the ligation of the common iliac. Blue spots did not appear until the day before death. Confer case 27.
18	I & II	Körte.	Deutsche med. Wchnschr., 1900.	1899, Apr.	Multiple aneurisms (aorta, ext. iliac, femoral, profunda); hemorrhage; organic lesion of heart; thrombosis fem. vein; ligation abdom. aorta.	+	—	Ruptured aneurism of the common iliac.	The bleeding (extravasation) continued after ligation of the common iliac. The aorta was tied to arrest the hemorrhage. Patient died on 37th day after the ligation of the common iliac, and one hour after ligation of the aorta.
19	II	Martin.	Brit. Med. Jour., 1903.	1901, Nov.	.....	—	—	Aneurism of external iliac.	Narrowly escaped gangrene as there were blebs and œdema of the toes. "Cure." Observed only 2½ months.
20	II	Maynard.	Indian Med. Gazette, Calcutta, 1903.	1903, Apr.	Extensive extravasation from rupture of aneurism; diarrhœa.	+	—	Diffuse iliac aneurism.	Circulation of limb not manifestly disturbed although the aneurism must have given off the epigastric, circumflex iliac and profunda arteries.

TABLE A.—Continued.

No.	Group.	Operator.	Published.	Date of Operation.	Complications.	Mortality.	Gangren.	Indication.	Comments.
21	I	Czerny.	Deutsche Ztschr. f. Chir., 1904 (Dreist).	1897, Feb.	Tuberculosis.	+	—	Slight hemorrhage in course of operation.	Collateral circulation chiefly by internal iliac arteries. The common iliac was tied for wound of a small anomalous branch of this artery occasioned in course of operation. Loss of blood, insignificant.
22		Küster.	Ibidem.	1898, Jan.	Ligation of both femoral and of right ext. iliac arteries.	—	—	Elephantiasis.	Ligation of left common iliac for cure of elephantiasis. Negative result.
23	I	Trendelenburg.	Ibidem.	1898, Oct.	Exsanguinating hemorrhage from accidental rupture of sac during the operation; general arterio-sclerosis.	+	—	Hemorrhage from dissecting aneurism of common iliac.	Death from hemorrhage.
24	II	Christel.	Ibidem.	1901, Mar.	Profuse hemorrhage during op.; extravasation of blood and infection; lig. ext. iliac and epigastric arts.	—	+	Spurious aneurism of femoral.	Aneurism of fem. art. and probably of the profunda. The ext. iliac ligated above epigastric and probably above circumflex iliac also. Amputation. Cure. Observed 2 years.
25	I	Clark.	Brit. Med. Jour., 1905.	1899, May	Repeated, severe hemorrhages to point of collapse; infection.	—	—	Hemorrhage.	One of the four cases in Group I of recovery after ligation of common iliac for hemorrhage, and the only case in this group (if we place Dequise's in Group II) recovered without gangrene. "Cure." Observed 9 months.
26	II	Cranwell.	Revista de la Sociedad Médica Argentina, 1906.	1904, Feb.	General arterio-sclerosis; great œdema of thigh and leg.	+	+	Aneurism of external iliac and femoral arteries.	Ilio-femoral aneurism. Profunda as well as epigastric and circumflex iliac arteries probably given off from the sac. Gangrene from toes to calf.
27	II	Gillette.	Annals of Surgery, Phila., 1908.	1906, Apr.	Lig. internal and external iliac arts.; sac opened and tied off; amputation for gangrene.	—	+	Aneurism of sciatic artery.	Confer case 17. Amputation.
28	II	Halsted.	Not hitherto reported.	1909, Jan.	.....	—	—	Ilio-femoral aneurism.	Aneurism cured. Observed 3½ years.
29	II	Beckman.	Communicated by letter, Mar. 6, 1912.	1912, Jan.	Enormously dilated femoral, ext. iliac and common iliac arteries.	—	—	Arterio-venous fistula of femoral vessels?	Employed Neff clamp, partially occluding the common iliac artery. Probably an arterio-venous fistula, caused by an operation for osteomyelitis of femur.
30	II	Judd.	Communicated by letter, Mar. 25, 1912.	1911, Dec.	.....	+	—	Aneurism of ext. iliac artery.	Employed Neff clamp, partially occluding the common iliac artery. Aneurism believed to have resulted from an operation for hernia performed six years previously.

TABLE B.—GANGRENE.

No.	Group.	Operator.	Additional factors in the production of gangrene.	Time of its appearance.	Indication for operation.	Comments.
1	II	Richter.	Huge aneurism; limb enormously swollen; patient very anemic.	Before operation. Extended to knee in 2 days.	Aneurism of external iliac.	Aneurism so large as to compel incision on opposite side of abdomen. Extraperitoneal operation.
2	II	Lange.	Aneurism ext. iliac and femoral arteries; leg cool, blueish and pulseless before operation.	.....	Ilio-femoral aneurism.	Cutaneous gangrene of great toe only. Due perhaps to the situation of the aneurism.
3	I	Kümmel.	Hemorrhage; ligation of ext. iliac (twice), of fem. (3 times), of epigastric, circumflex iliac, profunda, int. circumflex, ext. circumflex and comm. iliac arts.	11th day.	Hemorrhage.	There were no signs of gangrene prior to the ligation of the profunda and circumflex vessels, which were tied ten days after the ligation of the common iliac.
4	II	Schönborn.	Highly infected wound.	.....	Aneurism of external and internal iliac arteries.	Gangrene confined to the wound and its neighborhood.
5	I	Kümmel.	Multiple aneurisms; gangrene from rupture of aneurism in calf; hemorrhage.	Before operation.	Hemorrhage.	Desperate case.
6	II	Gouley.	Local and general infection.	19th day.	Ilio-femoral aneurism.	Published in 1885, but operated upon in 1871.
7	II	Smith.	Infection; thrombosis of ext. iliac, fem. and profunda veins, and of int. iliac, fem. and profunda arteries.	2nd day.	Fusiform ilio-femoral aneurism.	.....
8	I	Meyer.	Ligation of both int. iliac arteries; infection; hemorrhage.	.....	Hemorrhage.	Partial gangrene of toes.
9	II	v. Büngner.	Arterio-sclerosis; mitral systolic murmur; hemorrhage; excision of sac; exhaustion.	5th day.	Aneurism of sciatic artery.	Signs of gangrene (blue spots) appeared one day before death.
10	II	Christel.	Profuse hemorrhage during operation; ligation of ext. iliac and epigastric arteries; extravasation of blood; infection; enormously swollen thigh.	"After a time."	Aneurism of femoral and probably of profunda artery.	The ext. iliac was ligated above and below the epigastric and circumflex iliac arteries.
11	II	Cranwell.	General arterio-sclerosis; thigh and leg œdematous; patient in bad general condition. Compression by the aneurism of the internal iliac art.	3rd day.	Aneurism of external iliac and femoral arteries.	The internal iliac artery seems to have been greatly compressed by the aneurism of the external iliac. This may account, in part, for the gangrene. The aneurism involved the fem. as well as the int. iliac arts. and was of the fusiform variety.
12	II	Gillette.	Ligation of internal and external iliac arts.; excision of sac (ischiadic region).	3rd day.	Aneurism of sciatic artery.	The two cases of ligation of the common iliac artery in which an aneurism in the gluteal region was excised both had gangrene (cf. case of v. Büngner).

TABLE C.—FUNCTION IN CASES RECOVERED WITHOUT GANGRENE.

No.	Group.	Operator.	Date.	Time observed.	Function.
1	II	Mott.	1827	3½ months.	Patient states "leg is as strong as the other."
2	II	Salomon.	1837	10 months.	"Psoitis Rheumatica" (psoas abscess).
3	I	Deguise.	1840	5 weeks.	.....
4	II	Peace.	1842	14 months.	Able to work. Died of recurrence of aneurism (hemorrhage).
5	II	Hey.	1843	6 weeks.	.....
6	II	Garviso.	1843	.....	.....
7	II	Luzenberg.	1846	.....	No note as to function or time observed.
8	II	Bickersteth.	1862	37 days.	.....
9	II	Cock.	1863	'A few months."	"No untoward symptoms."
10	II	Jameson.	1885	6 months.	Flexed knee and hip.
11	II	Lucas.	1888	.....	.....
12	II	Stevenson.	1895	5 weeks.	.....
13	II	McBurney.	1897	3 months.	Weakness in left leg.
14	II	Martin.	1897	2½ months.	Could walk about slowly.
15	II	Küster.	1897	.....	Elephantiasis (operation for).
16	I	Clark.	1899	9 months.	Resumed work as porter at railway station.
17	II	Halsted.	1909	3¼ years.	Can walk only a short distance. Pain.
18	II	Beckman.	1912	2 months.	Arterio-venous fistula (operation for).

TABLE D.—THE MORTALITY AND ITS CAUSES.

No.	Group.	Operator.	Survived Operation.	Cause of Death.	Indication.	Comments.
1	I	O'Grady.	7 hours.	Previous operative procedures; hemorrhage; infection.	Arterio-venous aneurism of femoral vessels.	Operated upon in 1879.
2	II	Nicoladoni.	45 hours.	Prolonged operation; hemorrhage.	Spurious aneurism of right hypogastric and iliac regions.	Death might perhaps have been avoided by primary compression of the common iliac.
3	I	Kümmel.	12 hours.	Preoperative gangrene; hemorrhage.	Arrest of hemorrhage from one of a number of aneurisms.	Patient in desperate condition before operation.
4	I	Gouley.	21 days.	Pyæmia.	Diffuse aneurism of the ext. iliac.	Operation in 1871.
5	II	Fluhrer.	7 days.	Nephritis.	Aneurism of the external iliac.	The increase in blood-pressure may have lighted up a chronic nephritis.
6	II	Smith.	11 days.	Peritonitis (?); thrombosis; gangrene.	Ilio-femoral aneurism.	Ligation of the common iliac not alone responsible for the result.
7	II	Bryant.	3 days.	.....	Aneurism of the external iliac.	Very brief report. Cause of death not given.
8	II	v. Büngner.	5 days.	Hemorrhage; gangrene.	Aneurism of the sciatic artery.	The hemorrhage and gangrene might perhaps have been avoided by preliminary occlusion of the common iliac.
9	I & II	Körte.	37 days.	Hemorrhage; ligation of abdom. aorta 37 days after lig. of common iliac.	Ruptured aneurism of the common iliac.	Death occured one hour after ligation of the aorta.
10	II	Maynard.	8 days.	Extravasation of blood; preoperative gangrene of scrotum; diarrhœa.	Diffuse iliac aneurism.	Death not attributable solely to ligation of the common iliac.
11	I	Czerny.	5 months.	Miliary tuberculosis.	Slight hemorrhage in course of operation.	The ligation of the common iliac not responsible for the death five months later.
12	I	Trendelenburg.	3 hours.	Hemorrhage.	Dissecting aneurism of common iliac.	.....
13	II	Cranwell.	36 days.	Arterio-sclerosis; sacral decubitus; gangrene; amputation.	Aneurism of ext. iliac and femoral arteries.	The amputation wound showed no tendency to heal. Death too long after operation to be attributed to ligation of common iliac.
14	II	Judd.	2 days.	Patient did not rally from operation of 3 hours' duration.	Aneurism of external iliac.	Difficult and prolonged extraperitoneal ligation of the common iliac.

GANGRENE.

In the thirty-two cases operated upon prior to 1860, reported by Stephen Smith, gangrene of the leg or foot occurred in five or 15.6 per cent. But on study of the reports of these cases, I find that, probably, in only a single instance might the gangrene be attributed to ligation of the common iliac. The cases are as follows:

1. Group I. (No. 7, Smith.) G. W. F. Unde, Braunschweig. (Deutsche Klinik, No. 16, April, 1853.)

2. Group II. (No. 4, Smith.) M. Salomon, St. Petersburg. (Zeitschrift f. d. Gesammte Medicin, Bd. 12, Heft 3, 1839.)

3. Group II. (No. 5, Smith.) James Syme. (Edinburgh Medical and Surgical Journal, October, 1838.)

4. Group II. (No. 11, Smith.) A. J. Wedderburn, New Orleans. (New Orleans Medical and Surgical Journal, May, 1852.)

5. Group III. (No. 4, Smith.) C. Th. Meier, New York. (New York American Medical Gazette, May, 1859.)

Ad. 1. *Aneurism of the left gluteal artery; rupture of the internal iliac in attempt to ligate it; ligature of common iliac artery. Death on fourth day after operation.*

Autopsy.—"Internal iliac ruptured; indications of peritonitis, leg œdematous, calf red, showing signs of approaching gangrene."

In this case gangrene did not actually develop, notwithstanding the fact that the patient died on the fourth day. There were merely indications, and at the autopsy, of *approaching* gangrene. Had the patient lived, even these "signs" might not have manifested themselves. Note that the internal iliac artery was ruptured and not ligated and that five pounds of blood were lost. At autopsy the tissues about the sac were infiltrated with blood, and many pockets of blood were found in the muscles. Even, therefore, had gangrene developed during life, it would not have been attributable solely to the ligation of the common iliac.

Ad. 2. *Aneurism of the left external iliac artery; ligature of the common iliac. Recovery.*

The aneurism was traumatic, caused by the kick of a horse. It extended from four fingers' breadth above to the same distance below Poupart's ligament; in the region, therefore, in which important anastomotic vessels are located. The pulsation ceased and the tumor rapidly diminished in size after the ligation of the common iliac, and the limb which became cool at first regained its natural warmth. In this patient, nothing more than gangrenous eschars appeared on the foot which subsequently healed. It is to be noted that the situation of the aneurism in this case was approximately the same as in Wedderburn's (4), but in the former it may have been of the sacculated variety.[19]

The case is reported in great detail by Salomon in the quaint little Zeitschrift für die Gesammte Medicin, sometimes referred to as Oppenheim's Zeitschrift.

The patient died ten months after the operation from "psoitis rheumatica"—a suppurative inflammation in the course of the psoas muscle on the affected side.

Very instructive are the findings at autopsy relative to the collateral circulation after ligation of the common iliac. Salomon injected the descending aorta with a wax mass.

The injected wax mass had passed into both lower extremities. The arteria iliac communis sinistra had been ligated about one-half inch below the bifurcation of the aorta abdominalis, as was proved by the obliterated and narrowed portion of the common iliac; moreover, throughout its entire course, this artery was converted into a ligamentous substance; into the arteria iliaca externa sinistra some of the wax mass had been forced by way of the arteria hypogastrica sinistra (left internal iliac). The collateral circulation above the ligature had been carried on by means of the greatly dilated lowest arteria lumbalis (ileo-lumbar) whose branches communicated with those of the arteria circumflexa ilei sinistra. The left lower extremity received its arterial blood principally through the branches of the arteria hypogastrica sinistra, which communicated freely with those of the right side, so that the injected mass by way of these had penetrated into the vessels of the left thigh; the arteria femoralis was filled with wax to about two inches below Poupart's ligament. The arteria iliaca communis, iliaca externa and hypogastrica of the right side were greatly dilated. In the left thigh the branches of the obturator and ischiadic arteries were particularly enlarged.

These observations of Salomon's are instructive in that they demonstrate the importance of the obturator and sciatic arteries, of the anastomoses between the internal iliac arteries of the two sides, and between the circumflex iliac and ileo-lumbar arteries of the same side. No mention is made of the condition of the deep epigastric artery.

Ad. 3. *Aneurism of the right external iliac artery. Mortification of the limb and, subsequently, ligation of the common iliac artery.*

Here the gangrene preceded the operation and almost necessarily increased in extent after it.

Ad. 4. *Aneurism of the left femoral and external iliac artery. Ligation of the common iliac.*

Severe hemorrhage during the operation and death on the fourth day. Gangrene below the knee on the second day; extended to the hip on the fourth day. Pulsation ceased in the aneurism.

This was an aneurism which, perhaps, gave off all the important, anastomotic branches—the epigastric, circumflex iliac, profunda, internal and external circumflex arteries—above and below Poupart's ligament.

The great loss of blood during the operation may have enfeebled the patient to an extreme degree and predisposed to the gangrene, which was too great in extent to be conceived of as due solely to occlusion of the common iliac.

The original account of this case which was reported under the heading "Editorial"—"City Intelligence," is meager, and was, presumably, not written by the operator, Wedderburn. As to the findings at autopsy, nothing is said of the condition of the branches of the external iliac and femoral arteries nor is

[19] From Salomon's account of the post-mortem examination, "Die Pulsader-geschwulst hatte ihren Ursprung gleich oberhalb des Ligamentum Poupartii genommen und sich auf-und abwarts verbreitet."

the precise extent of the aneurism given. In the account of the operation, it is mentioned that the aneurism extended to within one or two inches of the bifurcation of the primitive iliac artery.

Probably there was extensive thrombosis of veins and arteries; and, as I have said, it is likely that all the arteries important for the anastomotic circulation opened into the aneurismal sac and became obliterated after the ligation. It is an established fact that the life of the limb may be imperiled by the cure, per se, of an aneurism.

Ad. 5. Patient, æt. 59. *Immense osteo-aneurism of the pelvis, gluteal region and femur. Ligation of common iliac.*

Second day, discoloration of the *wound and thigh;* third day, increasing discoloration; fourth day, wound dark and neighboring parts inflamed; toes and sole of foot black; gangrene continued to the hip. Gangrene appeared first about the wound. At autopsy, peritonitis was found. In this case, it would not be justifiable to assume that the ligation of the common iliac artery was alone responsible for the gangrene.

Only in Case 2, therefore, might it be reasonably supposed that the ligation of the artery was the sole cause of the gangrene; and in this patient there were merely eschars which healed without surgical interference. It is to be borne in mind that the wounds in all of these cases were infected.

To Stephen Smith's 32 cases (from 1827-1860) Kummel[20] adds 15 from the septic era.

To Group 1, 3 cases, from 1863-1865 (Nos. 13, 14 and 15). In none of these was there gangrene. In Case No. 14 amputatio femoris was done before the ligation of the common iliac and hence it is not pertinent to the subject under consideration.

To Group II, 12 cases,[21] from 1861-1875 (Nos. 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46). In only two of these (Cases 39 and 41) is mention made of gangrene.

Ad. 39. Hargrave.[22] *Arterio-venous aneurism of the external iliac vessels. Ligature of the common iliac artery.*

A large pulsating tumor of the left iliac fossa which had been treated in vain by digital and instrumental compression. On the 29th day after operation, dry gangrene of the foot began. On the 45th day all the toes were mummified. The gangrene extended, and the extremity became œdematous, as high as the hip joint. On the 67th day large pelvic abscesses were opened on both sides, and great quantities of foul-smelling pus evacuated. Arterial hemorrhage from the right abscess on the 71st day. On the 73d day recurrence of the hemorrhage and death.

Note that the aneurism was of the arterio-venous variety and probably included the epigastric and circumflex and iliac vessels, that there was very extensive suppuration in the pelvis, and that gangrene did not begin until the 29th day.

Ad. 41. Maundner.[23] *Ligation of the common iliac artery for aneurism of the right external iliac. Death on the 60th day from gangrene of the corresponding extremity.*

The common iliac vein was obliterated.

[20] Archiv. f. klin. Chirurgie, 1884, p. 66.

[21] Consult original article for Cases 57, 58, 59, 60, 61, 62 in Kümmel's appendix.

[22] Dublin Med. Press, 1865, Vol. II.

[23] Med. Times & Gazette, Oct., 1867 (Maundner).

From the years between 1875 and 1884, Kümmel reports only 4 cases (all antiseptically treated) of ligation of the common iliac artery, two being his own. Gangrene occurred in three (75 per cent) of these cases.

1. Group I. No. 16, Kümmel. (Archiv f. klinische Chirurgie, 1884, p. 67.)
2. Group II. No. 47, C. M. Richter. (Pacific Medical and Surgical Journal, 1881, p. 505.)
3. Group II. No. 48, Nicoladoni. (Sulzenbacher, Wiener med. Presse, 1882, Nos. 7-9.)
4. Group II. No. 56, Kümmel. (Loc. cit.)

Ad. 1. *Hemorrhage from erosion of the femoral artery, following operation for bubos, and diphtheritic infection of the wound. The femoral artery was ligated three times, the external iliac artery twice, and ultimately the profunda and circumflex arteries. Gangrene of the leg. Amputation. Recovery.*

Not only were all of the above vessels ligated, in addition to the common iliac, but the patient's vitality had been greatly lowered by repeated and excessive hemorrhages. Gangrene beginning in the foot on the day after the ligation of the profunda and the third ligation of the femoral (12 days after the ligation of the common iliac) had extended more than half way up the leg on the third day. In this case, certainly, the ligation of the common iliac artery was not alone responsible for the gangrene.

Ad. 2. *Aneurism of the external iliac. Ligature of the common iliac. Gangrene of the leg. Recovery.*

The aneurism, as large as the head of a child, was non-pulsating. The leg of the affected side was twice the size of the other. Ligation of the common iliac was undertaken because gangrene was beginning and the aneurism was increasing in size. Note that the gangrene antedated the operation.

Ad. 4. *Aneurism of the inguinal region and of the calf of the leg. Bursting of the latter aneurism. Ligation of the external iliac. Subsequent hemorrhage. Ligation of the common iliac. Death in 12 hours.*

Gangrene of the calf of the leg in the infiltrated tissues along the ruptured aneurism, occurred before the ligation of the common iliac artery. In not one of the three cases, therefore, was uncomplicated ligation of the common iliac artery responsible for the gangrene.

For the nine years from 1884, the date of Kümmel's paper, to 1903, the year of his own communication, Dreist was able to add only 6 cases to Groups I and II, none to Group III. One of these (Trendelenburg's) died of hemorrhage three hours after the operation. In two (Christel's and v. Varendorrf's) of the remaining five gangrene occurred (40 per cent), but it was not due, primarily, to ligation of the common iliac in either case.

1. Group I. (No. 3, Christel, 1901, loc. cit., p. 6.)
2. Group II. (No. 5, v. Varendorrf, 1898. Dissertation, Marburg, 1899.)

Ad. 1. *Spurious aneurism, presumably of the femoral artery, caused by splinter of iron. Ligation of the left, common iliac artery. Gangrene of leg. Recovery.*

Greatly emaciated patient; pulse 126-130; temperature 34.7°. Left thigh tremendously swollen, the tumefaction extending from knee to navel. In the course of the operation, the external iliac was twice ligated. The epigastric artery which was given off from the external iliac between the two ligatures was also ligated. Finally a ligature was placed on the common iliac artery; as further peril to the circulation of the leg there was deep suppuration of the œdematous thigh. To attribute the gangrene in this case to ligation of the common iliac would be unreasonable.

Ad. 2. *Injuries and aneurisms of the gluteal and sciatic arteries. Ligation of the left common iliac artery. Gangrene. Death.*

Woman, æt. 66. Pulsating tumor as large as a child's head in the left ischiadic region. Attempt made by the operator to ligate all the vessels contributing to the aneurism and to extirpate the sac (Philagrius). Accidental tearing of the sac. Ligation of the internal iliac artery which proved to be the seat of a fusiform aneurism. Immediately upon discovery of this, ligation of the common iliac artery which, in turn, presented several small, fusiform dilatations of its calcified wall. Extirpation of the sac and of two-thirds of the imbedded sciatic nerve. Tamponade. On the second day, gangrene of the entire leg. On the fourth day, death. The ligation of the common iliac was, accordingly, only one of the several factors which contributed to the gangrene.

In Kümmel's collection (1884), only four cases in Groups I and II are from antiseptic times (Nos. 2, 3, 5, and 7 of my Table A). As I have said, in three of these (two of them his own) gangrene occurred, but in two of the three the gangrene had manifested itself before the ligation of the common iliac. The number of his cases is too small for statistical purposes.

For Groups I and II in the antiseptic era, Dreist, 1903 (loc. cit.), collected ten cases—five for each group. Five of these had gangrene. Hence he concludes that "the chief danger" from ligation of the common iliac artery "is still today the gangrene which results in its consequence."

Gillette in 1908 (loc. cit.) could add only one case (Martin's) beside his own to the collection made by Dreist in 1903. He makes the statement that "gangrene of the leg has occurred in the last twenty-one cases seven times, or in 33⅓ per cent."

Matas, in a masterly article of 333 pages on the Surgery of the Vascular System (Keen's Surgery, 1909, Vol. V, p. 337), writing of ligation of the common iliac artery, says that "In the 21 operations done since 1880, presumably with antiseptic precautions, gangrene occurred 7 times, or in 33.33 per cent."

Gillette and Matas must have included in their calculations ligations of the common iliac artery performed with objects in view other than the arrest of hemorrhage and the cure of aneurism, cases complicated, some of them, by desperate operations such as disarticulatio inter-ilio-abdominalis, and which belong to the Groups III and IV of Stephen Smith.

In the thirty cases (Groups I and II) of ligation of the common iliac artery published since 1880, and collected in this paper, gangrene has occurred twelve times, or in 40 per cent (vid. Table B).

Table B has been arranged to enable the reader to see at a glance [21] the factors other than the ligation of the common iliac artery which have been instrumental in the production of the gangrene.

Two of the twelve cases (Nos. 1 and 5), can be excluded because the gangrene had manifested itself before the ligation of the common iliac was undertaken.

In one (No. 9) signs of gangrene ("blue spots") appeared on the fourth day when the patient, aged and exsanguinated, was almost moribund. She died the following day. In this case, the sac of a sciatic aneurism had been excised.

In Case 4 the gangrene, which consisted in the casting off of sloughs, was confined to the operative wound and its environs, and was due to an intense local infection. There was no gangrene of the foot or leg.

Perhaps the most striking instance in the literature of the extent to which the main arteries may be tied without manifest disturbance of the circulation of the limb is furnished by a case of Kümmel's (Table B, No. 3). In this patient, who was exsanguinated by terrific hemorrhage almost to the point of death, there were ligated the common iliac, the deep epigastric, and the circumflex iliac, the external iliac twice, and the femoral three times, and all without the production of signs of gangrene. It was not until eleven days after the ligation of the common iliac and when three vessels in the neighborhood of the profunda femoris had been tied, that gangrene supervened.

Gouley's case, No. 6, although not published until 1885, was operated upon in 1871, in the highly septic times. The patient died of infection on the 21st day, the gangrene manifesting itself not until 48 hours before death.

In No. 7, the case of Thos. Smith, there were, as complications resulting from infection, thrombosis of the external iliac, femoral and profunda veins, and of the internal iliac, femoral and profunda arteries. The aneurism involved the femoral as well as the external iliac artery and was of the fusiform variety. I should think that, in this locality, ligation of the common iliac for the obliteration of a fusiform aneurism might be more likely to be followed by gangrene than if performed for the cure of a sacculated aneurism, because from the fusiform variety, the deep epigastric, the circumflex iliac and the profunda arteries are given off, which they may not be in the case of the sacculated or spurious varieties (vid. also Cranwell's case, No. 11).

In Meyer's case, No. 8 (ligation of the external and both of the internal iliac arteries), infection and hemorrhage should be regarded as factors contributing to the gangrene which involved only the toes, and these only in part.

No. 10, Christel. In this instance it is clear that the complications must have been largely influential in the production of gangrene. Profuse hemorrhage occurred in the course of the operation. The external iliac artery was ligated both above and below the origin of the deep epigastric and circumflex iliac arteries, the latter of these being independently tied. There

[21] The reader is referred also to the abstracts which I have made of these cases.

was extensive extravasation of blood, the thigh was enormously swollen and the tissues infected. The aneurism was of the femoral artery and probably involved the profunda.

No. 12. Gillette ligated the internal and external iliac arteries, as well as the parent stem and excised an aneurism of the sciatic.

In ten of the twelve cases, therefore, it would be unfair, indeed absurd, to attribute the gangrene to the ligation of the common iliac artery.

The cases of Lange and Cranwell remain to be considered. In one of these, Lange's (No. 2), there seems to have been no complication and we must assign as cause for the gangrene the ligation of the common iliac artery. The gangrene was, however, very trivial, involving, as it did, only the skin of the great toe.

The situation of the aneurism may have been a factor in the determination of the gangrene. It involved the femoral as well as the external iliac arteries.

Cranwell's case (No. 11) is the only one known to me, operated upon in antiseptic times,[25] in which *significant* gangrene has occurred after ligation of the common iliac artery not complicated by other factors contributing to the serious disturbance of the circulation in the limb. The publication is in Spanish. The case seems to be fully reported and well presented and I have no reason for believing that there is anything to be read between the lines. As stated in the text and shown in a semidiagrammatic illustration, the internal iliac artery was compressed, possibly occluded, by the aneurism which involved not only the entire external iliac but also the femoral artery. It was noted before operation that the thigh and leg were œdematous, that there was general arteriosclerosis and that the patient's condition was bad. The aneurism had existed for fifteen and perhaps for thirty years. Attacks of cramps in the limb of the affected side, severe enough to prevent locomotion, had been present for thirty years (conf. abstract).

The case is a remarkable one, but must nevertheless be accepted for the present as furnishing an instance of the production of gangrene from ligation of the common iliac artery.

Granting that in the case of Lange and Cranwell the ligation of the artery was solely responsible for the gangrene, we have only two such cases in the thirty of my collection, a percentage of six and six tenths.

If it should appear later that Cranwell's case might, for unascertained reasons, be excluded, the percentage would, of course, be three and three tenths, and the sum total of gangrene the cutaneous necrosis of one toe.

The Anastomotic Circulation.

It would involve much labor to determine what the actual danger of gangrene is from ligation of the various arteries. The factors contributing to the gangrene in each reported case would have to be duly considered.

The percentages have been computed by many authors and although between the minimum and maximum estimates there may be great variation, there seems to be little doubt as to the relative frequency with which gangrene has manifested itself after ligation of one as compared with another of the principal vessels of the extremities.

There is abundant evidence in support of the view that, in a general way, the larger the artery, or the nearer it is to the heart, the less the impairment of the circulation attending its ligation. The subclavian, for example, may be tied quite without fear of gangrene, whereas from ligation of the axillary artery the circulation of the extremity is somewhat endangered, but not so much as from ligation of the brachial.

Peripheral gangrene has not been observed in consequence of ligation of the aorta. It may occur after ligation of the common iliac, has occurred much more frequently after ligation of the external iliac, and has followed ligation of the popliteal artery in a considerable percentage of the cases.

Kümmel, offering the generally accepted explanation of the imperfect law, writes:

> "It seems, naturally within certain limits, that the nearer the ligated vessel is to the central organ of the circulation, the easier it is for the collateral routes, *by means of the increased pressure from the heart*, to develop; this certainly seems to hold true of the vessel which we are considering (common iliac).
>
> "Astonishing as it may seem, it nevertheless appears to be a fact, as already stated, that the ligation of the common iliac less endangers the vitality of the lower extremity, and makes easier the establishment of the collateral circulation than does the ligation of a peripheral vessel, for example, the external iliac.
>
> "I do not hesitate, therefore, in the case of aneurisms of the external iliac and high femoral arteries, to express a preference for the ligation of the common iliac, even when ligation of the external iliac is possible, for, thereby, the definite cure of the aneurism seems to be more certain of accomplishment, and the life of the limb is less endangered."

Surely one would not, with the hope of diminishing the danger of gangrene and in order to produce a condition equivalent to the tying off of the parent trunk, ligate the internal iliac after ligation of the external iliac had been made. Ligation of the common iliac is not, of course, equivalent to ligation of the external and internal iliacs, unless one or the other of these branches is obturated at a lower point, as by aneurism; or unless they are ligated so close to the parent stem that no blood can pass from one to the other over the spur of bifurcation.

May it not be, inasmuch as in the cure (spontaneous or operative), per se, of certain aneurisms there lies danger to the life of the limb, that the particular situation of the aneurism may be an important factor in the determination of gangrene, and that, for example, the aneurisms for the cure of which ligation of the common iliac has generally been done are less likely to impair the vitality of the limb than are the aneurisms for which ligation of the external iliac has usually been undertaken?

The obliteration by any method of ilio-femoral aneurisms giving off the deep epigastric, circumflex iliac and profunda arteries might well be followed by impairment more or less serious of the circulation of the foot and leg, whereas the cure of an aneurism of the external iliac artery terminating above

[25] Antiseptic precautions were presumably observed.

the origin of one or more of these branches should not be attended with equal consequence.

As shown by Porta,[26] Pirogoff[27] and Kast,[28] and as observed by myself, the epigastric and circumflex arteries are of great importance in the establishment of the collateral circulation after ligation of the abdominal aorta. Salomon and Czerny have emphasized the great dilatation of the internal iliac and its branches after ligation of the common iliac artery. The anastomoses between the two internal iliacs are very free and numerous, and through these the blood reaches the femoral artery chiefly by way of the profunda. I have already called attention to the interesting fact that in Kümmel's case (Table A, No. 5) the circulation of the limb remained good until the profunda and its circumflex branches were occluded, although the common iliac, the external iliac (twice) and the femoral (three times) had previously been ligated.

We find additional demonstration of the importance of the anastomoses between the internal iliac arteries of the two sides after ligation of the common iliac in the two cases of our collection in which the sac of an aneurism in the gluteal region was excised. In both of these gangrene supervened.

Ligation in continuity should rarely be resorted to, for when branches are given off between the sac and the ligature, the circulation of the limb is more impaired than by ligation, tangential to the sac, and for the reason that the artery becomes obstructed in two places, at the site of the ligation and of the aneurism.

Partial Occlusion.

It may be asked, "What is to be gained by partial occlusion of the common iliac, if its object is the cure of the aneurism and obliteration of the arteries given off from the sac?" The reply is that with the partial occlusion of the parent trunk, the direct circulation through the internal iliac is not obturated. I believe, however, that the common iliac artery, partially occluded by a metal band, will ultimately become completely obstructed. My experiments on the aorta of dogs afford ample proof for the belief that even a small direct stream is of great value. Thus a considerable mortality attended the complete occlusion of the aorta in dogs, whereas with partial obstruction by the metal band, death rarely occurred. In man, I have in four instances had the opportunity to observe the effect of partial occlusion of the aorta. In no case were disquieting symptoms manifested, although in one patient the femoral pulse was obliterated by the partial obstruction and reappeared only on agitation or exertion.

These results are in striking contrast with those consequent to ligation of the aorta.

A fusiform aneurism of the aorta was so greatly reduced in size by partial occlusion with the metal band that relief from the symptoms was obtained and the aneurism was believed to have been almost cured. But the patient died in six weeks from a sudden hemorrhage due probably to atrophy of the diseased arterial wall and the cutting through of the band.

A band was applied one and a half years ago to a greatly dilated vein proximal to an arterio-venous fistula, which had been painstakingly explored in the hope that the opening might be closed without obliteration of either the vein or the artery. The patient, an old man, with advanced arteriosclerosis, has recently sent me word by his physician, Dr. Fox of Greenville, Tenn., that his condition is greatly improved by the operation.

The partially occluding metal band has already been applied by me in man to all of the principal arteries, to the aorta four times; innominate, once; subclavian, twice; carotid, many times; femoral, three times; popliteal, once; and without accident except in the aortic case, referred to above, which will probably be reported later by the eminent director of a European clinic.

The partial occlusion, with a metal band, of an artery, other than the aorta must, ultimately, it seems to me, bring about total obliteration of its lumen. Occasionally the aorta becomes converted, under the band, into a solid fibrous cord. This has occurred, thus far only in cases in which the vessel was almost completely occluded.

But I have been constantly apprehensive lest, in the case of the aorta, the wall might ultimately give way, atrophying slowly but surely, under the pressure exerted by the constricting metal. As our laboratory for experimental surgery is closed during the summer, it has not been feasible for me to observe the ultimate effect of a partially occluding band upon the aorta for a period longer than 7½ months. In many instances, however, I have noted a thinning of the aortic wall under the band, and in some the attenuation has been so great that I could foresee no outcome other than perforation of the wall of the artery.

In total occlusion of the artery the band in three animals was found embedded in a strong, fibrous capsule continuous above and below with the arterial wall. In this manner hemorrhage was prevented, notwithstanding the fact that the aorta as well as the fibrous capsule were patulous throughout. The band was, however, so snugly embraced by the surrounding cylinder of fibrous tissue that little, if any blood could pass between the two.

But in the cases of partial occlusion of the aorta no such fibrous capsule was forming, and for the reason, undoubtedly, that there was no occasion for its formation. The occasion would, probably, come sooner or later, and perhaps, altogether without warning, or too quickly for efficient response from the surrounding tissues.

Hence, if a partially obstructing metal band is applied to the aorta, it would seem that some further operative procedure must usually be contemplated, even if the aneurism should be apparently cured. It might consist in partial occlusion of both common iliac arteries (this might be done as part of the original operation) and later of complete occlusion of the aorta, by bands or possibly ligatures, both above and below the

[26] Della Alterazioni Patologiche Della Arterie Per La Ligatura E La Torsione. Esperienze Ed Osservazioni Di Liugi Porta. Milano, 1845.

[27] Pirogoff. Journal der Chirurgie und Augenheilkunde. v. Walter und v. Gräfe, 1838, XXVII.

[28] Kast, Deutsche Zeitsch. f. Chirurgie, XII, 405.

original band. In the cases in which it may be ventured to close the aorta almost completely, the fibrous-cord formation might be hoped for, and the omission of a second operation justified.

We noted further in our experiments that the aorta of dogs after having been totally occluded by silk ligature may again become patulous. This restoration of lumen is brought about by the cutting through of the ligature, and has usually been accompanied by the formation of a diaphragm of greater or less extent.[29] Similar observations have been made upon the human subject after the ligation of large arteries (innominate, subclavian, femoral).

Acting on this hint given by nature, I tested, last winter, on thirteen dogs, the effect of partially occluding ligatures of fine silk, placed one above the other on the aorta, hoping that we might obtain a series of superimposed diaphragms which, if sufficient in number and extent, might sufficiently obturate the aorta to bring about the cure of an aneurism.

But these partially occluding ligatures of very fine silk, not only produced no diaphragms, but gave rise in two of the thirteen dogs to fatal hemorrhage.

From the totally occluding, crushing, coarse, silk ligature in dogs, I have seen no case of hemorrhage. Was, then, the fineness of the silk or the incompleteness of the occlusion responsible for the bleeding? Or were both concerned in bringing about the result?

We are now testing the behavior of organizable tissues used as bands to constrict the aorta. Spiral strips and cuffs cut from the fresh aorta of one dog are wound about the aorta of others. I should fear, however, that tissues capable of organization under such circumstances would be stretched * by the dilating force of the aortic pulse. Should they serve their purpose for a time, enough might possibly be accomplished to enable one at a subsequent operation to produce, if necessary, complete occlusion in some other way.

Lateral excision of a piece of the aortic wall and suture of the defect might easily be accomplished experimentally, but in the presence of aneurism this would, I fear, rarely be feasible; for the aneurism usually occupies so much space that there is not sufficient room above it, for example, between it and the renal arteries, for the carrying out of any such measure. Ordinarily it would be difficult to obtain more than room enough for the application of a band.

Function.

Unfortunately there are not sufficient data to enable me to formulate conclusions as to the ultimate usefulness of the limb after ligation of the common iliac.

In Table C is embodied all that we have learned in one hundred years concerning the function of the limb following this operation.

Seven of the thirty-two cases tabulated by Stephen Smith recovered. One of these (Guthrie) belongs to Group III. Of the remaining six cases, one (Deguise) is in Group I, five (Mott, Salomon, Peace, Hey, Garviso) are in Group II.

Deguise's patient left the hospital in five weeks. There is no note of subsequent observation. For the study of function

[29] Jour. of Exp. Med., 1909, Vol. XI, No. 1.

* June 3, 1912. Since going to press one of two dogs operated upon April 29 for the purpose of testing the effect of cuffs and of spiral strips of the fresh aorta of one dog wound about and constricting the aorta of others we examined to-day under ether, and to our delight and surprise found that the aortic cuff which had been used in this experiment seemed to be completely organized and had not, apparently, stretched in the least. The aortic pulse immediately above the constricting cuff was forcible; just below the cuff it was feeble but countable, and at this point a barely perceptible thrill was appreciable. The left femoral pulse could with difficulty be felt and counted by Dr. Goetsch who with Dr. Jacobson assisted me in making the examination, but on the right side (smaller artery) it was questionable whether or not the pulse could be appreciated with the finger. Having clamped all the aortic branches up to the band, it was noted on removal of the clamp from one of the common iliac arteries that the blood trickled feebly and with barely perceptible pulsation from the open end of the vessel. On dissecting the aorta after removal from the body, it was ascertained that the cuff which seemed, as it were, welded to it had not stretched or become thinned or altered in appearance. A fine probe passed into the aorta was snugly embraced at the site of the cuff. The artery was split open at both ends up to the cuff and the fine opening and characteristic wrinkling of the constricted vessel noted. There was almost no reaction about the cuff which seemed to be organized. Even its free flaps had retained their original dimensions.

Another dog, operated upon on the same day and in the same manner, except that a spiral strip of aorta instead of a cuff was used for the band, died suddenly about three weeks after the operation. In this instance the aorta had been almost completely occluded by the spiral band the turns of which had been held by three fine silk sutures, two applied at the pointed ends of the spiral strip and one near its middle. Dr. Jacobson, who kindly took charge of the dogs after operation, removed the specimen which I have just examined. The findings are precisely the same as in the first case. The weld-like band had not stretched, and the aorta, on being split longitudinally, was seen to be greatly wrinkled and almost occluded at the site of the seemingly organized spiral strip. There was no adhesion between the folded intimal surfaces which had been so firmly held in contact.

Thus, perhaps, at last, a safe and reliable method for occluding the aorta has been found, and an interesting and promising field for investigation opened.

Fresh tissues of other kind may serve the purpose quite as well as the aortic cuffs or strips. This remains to be determined. We await the findings of the histological examination of the specimens with much interest.

In similar manner, with bands of fresh tissue, partial and complete obstruction and isolation of the intestine might be produced.

this case might be considered under Group II, for the operation which resulted in the ligation of the common iliac was undertaken for the cure of an inguinal aneurism. It was only in the course of the operation that hemorrhage necessitating the ligation of the common iliac occurred. (Vid. Am. Jour. Med. Sc., Oct., 1841, p. 475.) If this case were transferred to Group II, the mortality for ligation of the common iliac prior to 1860, would be one hundred instead of ninety-one per cent.

Mott's patient, observed 3½ months, stated at the end of this period that his leg was as strong as the other. While the memories of the agonizing pains suffered before the operation were still vivid, it is supposable that he might in his joy at being relieved of his torture and in his desire to emphasize his gratitude to his deliverer have overestimated the relative usefulness of the limb.

It will be observed that my patient, operated upon three and a half years ago wrote enthusiastically of the result a year after being cured, but now realizes that he is considerably incapacitated. Salomon's patient died ten months after the operation from a suppurative inflammation in the course of the psoas muscle on the affected side. It is stated that the patient of Peace was able to provide for his family, pursuing the arduous occupation of loading boats with stones. But about 14 months after the operation, a small, soft, non-pulsating tumor appeared at the site of the aneurism. Perforation of the skin and hemorrhage took place in a few days and in eleven days thereafter he died.

Nothing is known of the cases of Hey and Garviso after leaving the hospital.

Kümmel adds to Smith's list two cases of cure between 1860 and 1880 (McKinlay's, Group I, and Cock's, Group II).

McKinlay's case is not pertinent for the study of function, for the thigh was amputated. In Cock's case there is a note that when seen "a few months after leaving the hospital there were no untoward symptoms," and that he resumed his occupation.

Hence for the septic period only one case (Peace, 14 months) was observed long enough to be considered in estimating the usefulness of the limb.

Of the thirty cases of the antiseptic period, fourteen died. Of the remaining sixteen, seven had gangrene. Of the nine without gangrene (and these, of course, are the only ones to be considered under the heading of function) there is in two (Lucas and Stevenson) no record of observation after the discharge from the hospital. In one (Küster) the operation was performed on a patient incapacitated by elephantiasis. Of the others, Beckman's was observed for two months ("improved"), Martin's for two and one-third months ("could walk about slowly"), McBurney's for three months ("weakness in left leg").

At the end of six months, Jameson's patient walked with difficulty. The hip and knee were flexed.

Clark's patient, observed for nine months, worked as a porter, wheeling a barrow about a railroad station.

My patient is still under observation, three and one-quarter years since the operation. April 4, 1912, he wrote me, "My left leg is a great deal weaker than my right. I can't walk very much as I have pain in my left leg when I do any walking and in case it gets very cold. My present weight is 180 pounds. I have a splendid appetite and haven't been ill since my return. All traces of the aneurism have disappeared and it never worries me the least bit."

Mortality.

Stephen Smith in reviewing the result in the cases of his first group writes:

> "Of 11 cases, 10 were fatal, one recovered, being a mortality of nearly 91 per cent. The success of this operation upon the primitive iliac artery for the causes above assigned, presents a striking contrast with the operation upon the external iliac for the same class of diseases and accidents. Of 14 cases of deligation of the external iliac artery for the arrest of hemorrhage, I find that 11 were successful and three fatal, the mortality being about 21½ per cent."

Concerning Group II, he remarks:

> "A just appreciation of the results of these 15 cases would give the following conclusions: recoveries, five; permanently cured, one (Mott); temporarily, two (Salomon, Peace); unknown, two (Hey, Garviso); died, ten; fault of ligature, one (Crampton); condition of patient most unfavorable at time of operation, two (Syme, Van Buren); intercurrent disease unconnected with operation, one (Stone); connected with operation, three (Stevens, Jones, Wedderburn); local disease due to operation, one (Stephen Smith); cause of sinking and death uncertain, one (Goldsmith); attributed to operation, one (Lyon).
>
> "The results of the operation of deligation of the common iliac artery for aneurism, as compared with the same operation upon the external iliac, is worthy of notice. In 95 cases, which I have examined, of ligation of the latter artery for aneurism, 69 recovered and 26 died, being a mortality of about 27 per cent, or less than half the mortality of the same operation for the same disease when performed upon the common trunk. The cause of death in 11 cases, or nearly one-half, of ligation of the external iliac for aneurism was mortification of the limb, presenting a striking contrast with the same operation upon the primitive iliac, in which there was but one instance in eight cases."

Dreist collected 52 cases from the septic era; 17 of these are in Group I; 14 died; mortality 82.35 per cent; 35 are in Group II; 26 died; mortality 74.29 per cent. From the antiseptic era (since 1880) he collected 10 cases; five in Group I, with three deaths; mortality 60 per cent; five in Group II, with three deaths; mortality 60 per cent.

I have compiled for the hundred years from 1812 to 1912 (Groups I and II) 76 cases of ligation of the common iliac. Hence three-quarters of a case per year since the first ligation by Gibson. 46 of these were operated upon prior to 1880 (septic era); 30 subsequent to that year.

Sixteen are in Group I; of these three recovered; mortality, 81.3 per cent. Sixty are in Group II; recovered 25; mortality, 58.4 per cent. Of the 30 cases, Group II, of the septic period, 21 died; mortality 70 per cent. Of the 30 cases, Group II, of the antiseptic period, 14 died; mortality 46.6 per cent.

Analysing the 14 fatalities since 1880 (vid. Table D), we find that in three cases only (Fluhrer, Bryant and Judd)

could death be attributed solely to the ligation of the common iliac artery. In all the others there were serious complications, sufficient to account for the fatal termination. In Fluhrer's patient nephritis is given as the cause of death. In Bryant's, no cause is assigned; the report, however, is very brief. Judd's patient did not rally from the shock of the prolonged (three hours) operation. The mortality, therefore, in the uncomplicated cases is at most 10 per cent. Possibly it is only 3.3 per cent.

Epicrisis.

From the critical consideration of the cases collated in this paper we may, I think, conclude that the uncomplicated ligation of the common iliac artery is not likely to be followed by gangrene, the percentage being from 3.3 to 6.6 instead of 33.3; and that the mortality, contrasted with 60 per cent as estimated by Dreist for Groups I and II, is at most 10 per cent and probably not more than 6.6 per cent; or it may even be as low as 3.3 per cent.

The data are too meager to justify an expression of opinion as to function, my patient being the only one observed for sufficient time. In this man, although there may be no visible signs of disturbed circulation, the fact that he is unable to walk further than a very short distance without cramp-like pain would seem to indicate that the impairment of function should be attributed to ischæmia of the limb.

In Clark's case, at nine months, the function seems to have been good. His patient was only 26 years old.

Notwithstanding the low mortality and the infrequency of gangrene consequent upon ligation of the common iliac for aneurism, the operation is not an ideal surgical procedure, and chiefly, in my opinion, for the reason that it cuts off the direct blood supply from the internal iliac.

Furthermore, the operation under consideration does not invariably cure aneurism. In the eleven cases of recovery since 1880, without gangrene, and in which the operation was performed for aneurism, there was recurrence in one after seven months (Gillette), and of the six cases in Stephen Smith's collection, one recurred after fourteen months (Peace). It is possible that in other cases, also, recurrence would have been noted had the patients been observed for a longer period.

In extirpation of the aneurism we have a means of curing it. But that this procedure, which has rarely been resorted to in the case of aneurism of the external iliac artery is less dangerous, or less or more liable to be followed by gangrene, we do not as yet know. We might, however, predict that the function of the limb would be less impaired by the excision of the sac than by the ligation of the common iliac, because the former operation does not interrupt the circulation in the internal iliac artery.

In the excision of such an aneurism the external iliac would have to be ligated twice and if the lower ligature had to be placed below the deep epigastric and circumflex iliac arteries, the limb would be deprived of the services of these important anastomotic channels. We know, as I have said, but only in a general way, that ligation of the external iliac is much more likely to be followed by gangrene than is ligation of the primitive stem.[30] Furthermore, the enucleation of an aneurism may be difficult and attended with the danger of wounding important veins and of thrombosis of vessels not actually cut or torn.

The ideal operation, as it seems to us at present, is one which causes only so much disturbance of the circulation as is necessarily incident to a spontaneous cure of the aneurism, namely its obliteration.

This is precisely what the Matas operation contemplates. The vessels which are given off from the sac must, in the course of cure, be occluded at their origin, and, presumably to the first collateral branch.

I should suppose, however, that the danger of gangrene after the Matas operation would be at least as great as from ligation of the afferent artery immediately above the aneurism, were it not that the former procedure promptly relieves the patient of the tumor and the pressure which it exerts, whereas after ligation many months may be required for the absorption of the aneurism. Also in favor of undertaking to perform the Matas operation, even in cases which might prove to be unsuitable for it, is the fact that the precise state of affairs becomes investigated and such endeavor not infrequently may result in the finding of a hole in the artery, as in the case of Balch and Murphy,[31] the closure of which will suffice to cure the spurious aneurism. In such case, although the performance of the Matas operation is not indicated and, indeed, not possible, the result will justify the means.

In other words, the condition of the patient permitting, a thorough operative investigation should be made in all cases of aneurism or wound of the external iliac artery.

A fatal termination might have been avoided in a very considerable number of the cases of ligation of the common iliac if this vessel had been temporarily compressed and the precise condition investigated at the first operation.

I should not suppose that the preservation of the vaso vasorum would be important for the prevention of gangrene which, when it occurs, follows operation too quickly for these little vessels to have become serviceable. Maintenance of their integrity might possibly be of value for the preservation of function.

In what has been said, I have not had in mind either the restorative or reconstructive operations of this eminent surgeon. The former of these procedures may have a sphere of great usefulness in saccular and arterio-venous aneurisms, but I have not regarded with much favor the attempts which have been made to reconstruct arteries from the diseased wall of the aneurism. I believe it will be found that modification of the Matas operation may be indicated in many cases, possibly in a considerable proportion of them. It may, for ex-

[30] It would be interesting to try to determine by careful study of the cases, the explanation of this well established fact. It is my opinion, as already indicated, that it may be found in the situation of the aneurism.

[31] Boston Med. & Surg. Jour., 1908, Dec. 24, p. 800.

ample, not always be desirable, even when possible, to approximate the intimal surface throughout. In some cases it may seem better to split the sac longitudinally or otherwise, in one or more places, and to close the several parts of the sac independently. In others the sac may lend itself in part or in toto to excision naturally and without injury to outside vessels, and when this is the case enough of the sac might be left on the stump of the various arteries to enable the surgeon to close their orifices, from the intimal side, if it should seem advisable to do so, with one or more circular stitches or rows of suture.

In cases in which no advantage is to be gained by leaving the sac, it might, perhaps, better be removed. It should, in my opinion, never be drained merely for the sake of drainage. It is conceivable that in rare instances it might have to be packed for the control of hemorrhage, as, for example, in a case of spurious aneurism, when, if the patient were exhausted, it might be unwise to attempt to check every oozing point.

In the case of subclavian aneurisms I am still of the opinion that excision when feasible may prove ultimately to be the best treatment in selected cases. When the sac lends itself easily to enucleation without danger to the contiguous vessels, there should be no added danger attending its extirpation. All of the arteries arising from it can be ligated as they present themselves in the course of the dissection—arteries which in the performance of the Matas operation would either have to be exposed and temporarily clamped, or occluded, less advantageously perhaps, and at times with difficulty in the presence of hemorrhage, from within the sac. In many instances the operators have been greatly embarrassed on opening the sac by hemorrhage from vessels which were not or could not be clamped from without.

Of the cases not located on the extremities, those lend themselves best to the performance of the Matas operation in which all of the arteries leading from the sac can be temporarily clamped outside of it. Now when all of these have been exposed sufficiently for clamping it is not quite clear to me why their permanent closure should be deferred until the sac shall have been opened.

A few days ago, in operating upon an aneurism of the dorsalis pedis artery, the afferent and efferent orifices were less than 1 cm. apart and were easily approximated without tension. An end-to-end suture which in some situations and under certain conditions would be unquestionably indicated was not considered worth while, and it would have seemed absurd not to have excised the readily enucleable sac.

Each aneurism presents its special problems which it may not be possible to solve altogether until the operation has neared completion.

As a general proposition, I should be disposed to ligate permanently, just outside of the sac, all arteries which in the natural course of performance of the Matas operation would be clamped temporarily. And, inasmuch as all arteries leading from the sac should, when feasible, be under the control of clamps (when not controllable by the elastic bandage) before the sac is opened, are there good reasons for not removing under these circumstances a sac which has, in the process of the exposure of the arteries for clamping, become almost enucleated?

I have been unable as yet to convince myself that arteries which have been temporarily occluded in close proximity to the aneurism might not better be tied at once and divided, for thus the arteries still to be sought with the object of temporary occlusion in view become more readily accessible. And when these secondary arteries have been clamped why not ligate and divide them also for the same reason, and so on until all of the arteries, which in the course of the Matas operation would be temporarily occluded, have been tied off?

So much of the sac as, by this time may have been dissected out, might, it seems to me, be removed with advantage unless it could serve some special purpose by being left.

And even in the cases in which the Matas operation seems to be clearly indicated and in which temporary compression of the main artery above and below the sac is contemplated, the dissection necessary for an exposure of this vessel which would be ample for the simple ligation might be insufficient for its temporary occlusion with the necessarily somewhat cumbersome clamps designed therefor.

In the case of popliteal aneurisms especially, and of aneurisms so situated that their blood supply can be completely controlled by tourniquet the Matas operation plays an important rôle. In brief it is particularly applicable to the treatment of such aneurisms of the extremities the extirpation of which might be attended with greater interference with the circulation. In other situations, in the case of easily enucleable aneurisms, the danger of hemorrhage should ordinarily be less with extirpation than with the Matas operation.

Dr. Matas has with great courtesy written me concerning the cases of aneurism of the external iliac and ilio-femoral arteries which have been treated by his method and I await with interest their publication in detail. No one, I am sure, can be more eager than he to determine the precise indications for the operation so brilliantly conceived by him or to suggest modifications of it should they seem to be clearly indicated.

It is undoubtedly the duty of every surgeon to familiarize himself by much practice on animals with the treatment of wounds of the heart and largest blood vessels, veins and arteries, for otherwise he might be unable to cope properly with an emergency which, any day, may confront the active practitioner of this art. I would recommend the making of fistulæ between the aorta and vena cava, the vena cava and portal vein, and between the innominate vessels. Also the practice of the end-to-end suture and the implantation of vessels.

One of the chief fascinations of surgery is the management of wounded vessels, the avoidance of hemorrhage. The only weapon with which the unconscious patient can immediately retaliate upon the incompetent surgeon is hemorrhage. If he bleeds to death, it may be presumed that the surgeon is to blame, whereas if he dies of infection, or shock, or from an unphysiological operative performance, the surgeon's incompetence may not be so evident.

NOTES ON NEW BOOKS.

Nervous and Mental Diseases. By Archibald Church, M. D. and Frederick Peterson, M. D. Seventh edition. Revised. Illustrated. $5.00. (*Philadelphia and London: W. B. Saunders Company, 1911.*)

Comment upon a work which has reached a seventh edition seems superfluous. Evidently the book finds an appreciative public. A number of changes have been made in this edition which are improvements. The chapters on Meningitis, Aphasia, Poliomyelitis, Pellagra, and Pituitary diseases have been largely rewritten. A section upon Oppenheim's Congenital Amyotonia has been added and a brief account of the various theories as to the nature of Hysteria. Descriptions of the conditions due to reduced pituitary activity have been briefly interpolated, strangely enough, with but scant mention of Cushing's work. In the section upon Mental Diseases the résumé of the principles advanced by Wernicke, Ziehen, and Kraepelin which graced the fourth edition and which was written by Meyer, has been omitted. Possibly this was found to be too advanced for the public appreciating this work.

Judged from the standpoint of the student and practitioner, for whom this work was written, the present edition is fully up to the standard. There is much more to commend than to criticise. Numerous illustrations of an exceptionally excellent character add greatly to the usefulness and attractiveness of the book.

W. R. D.

Diseases of the Stomach. With Special Reference to Treatment. By Charles D. Aaron, Sc. D., M. D. Illustrated. $4.75. (*Philadelphia and New York: Lea & Febiger, 1911.*)

Nearly one-half of this work is introductory to the chapters dealing with the actual diseases of the stomach. The author first discusses the physiology of digestion, the examination of the stomach, contents, diet, methods of treatment, etc., and then passes on to the consideration of the various neuroses of the stomach to which he devotes about a hundred pages, and the final one hundred and fifty pages to the more strictly organic diseases. Treatment, as indicated in the title, is the part on which the author lays most stress, and from this point of view the average practitioner will find the book useful. The book does not add to our knowledge of stomach diseases, but the author has gathered much information together in a clear way and written a work which will doubtless prove attractive to the students from its simplicity.

Dysentery in Fiji, During the Year 1910. By P. H. Bahr, M. B., etc. Supplement No. 2 of The Journal of the London School of Tropical Medicine. Illustrated with Plates and Charts. 6/. (*London: Wetherby & Co., 1912.*)

This short monograph is important as it adds to our knowledge of the prevalence of one of the common tropical diseases in a country with which there are large commercial relations, and from this point of view such reports are of very distinct value. The more detailed information we have in regard to the existence of a disease, the greater is our power to control it, and to prevent those exposed to it contracting the malady. Such a study is one of the best results of the school which gave birth to it.

Compendium of Diseases of the Skin. With a Therapeutic Formulary by L. Duncan Bulkley, A. M., M. D., etc. Fifth Revised Edition. $2.00. (*New York: Paul C. Hoeber, 1912.*)

Under a new name Dr. Bulkley presents his manual which has been so widely known and appreciated for many years, especially by the student and general practitioner. As a result of the wide experience of the author his therapeutic formulary is most helpful, as the treatment of skin diseases is usually a serious stumbling block for the physician. Dr. Bulkley's description of diseases is brief but clear, and as a very concise manual there is none better in English.

The Technique and Results of Radium-Therapy in Malignant Disease. By M. Domenici, M. D., Paris, and A. A. Warden, M. D., Glasgow and Paris. 75 cts. (*London: J. and A. Churchill; Philadelphia: P. Blakiston's Son & Co., 1912.*)

This is merely a very brief reprint of an article from the British Medical Journal, 1910, with additional plates and more recent notes. It is interesting as showing the success attained by this means of therapy in a few cases, only seven, of lymphadenoma, sarcoma, and epithelioma.

Duodenal Ulcer. By B. G. A. Moynihan, M. S. (London), F. R. C. S. Second edition, enlarged. Illustrated. $5.00. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

On its first appearance this book was favorably reviewed in our columns (August, 1910), and it is not at all surprising that a second edition has been called for. Dr. Moynihan has made this disease a life-long study, and the results of his work are invaluable to other surgeons. "The changes in the text in the second edition of this work have been chiefly concerned with the differential diagnosis of duodenal ulcer and the result of X-ray examinations of the stomach after the administration of bismuth." (Preface.)

Treasury Department. Public Health and Marine-Hospital Service of the United States. Reprint from Public Health Reports, No. 70. Municipal Ordinances, Rules and Regulations Pertaining to Public Hygiene. Adopted from January 1, 1910 to June 30, 1911, by cities of the United States having a population over 25,000 in 1910. (*Washington: Government Printing Office.*)

This pamphlet will be of very great service to the governing boards of town and cities, and to many organizations interested in public hygiene. The study of what has been accomplished by others shows us how much we can do ourselves, and the example set by some cities in bettering social conditions is a great stimulus to others in undertaking similar or new work. These rules, etc., cover the questions of communicable diseases, poliomyelitis, vaccination, spitting, street cars, drinking cups, food stuffs, milk, meat, garbage and a number of other vital problems. It is a satisfaction to note how the cities are awakening to the importance that all these questions have for the health of their citizens.

Pellagra. By George M. Niles, M. D., Professor of Gastro-enterology and Therapeutics in the Atlantic School of Medicine, Atlanta, Georgia. Illustrated. $3.00. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

Up to a very recent time there was good reason why pellagra should not be recognized by the average practitioner in the regions where it mainly was seen. It had not been described as an American disease, and its various stages and forms did not appear to group themselves together, so as to become a recognizable unit. But from now on there will be less and less excuse for mistakes being made in the diagnosis of this disease. Already several works on the subject have appeared in English, and with this last addition to the bibliography, every physician has the means to become thoroughly acquainted with the symptoms. It is to be hoped that the doctors throughout the south will study Dr. Niles' book with care, for he presents the matter in a clear and interesting way. He is a firm believer in the zeist theory of the origin of the

disease, and whether the future proves this to be the real cause or not, does not diminish the value of his book. There is much uncertainty still, in spite of all the foreign studies of pellagra, in regard to various features of this disease, but the author gives all the evidence at hand, especially in regard to the mental symptoms, which may help to enlighten the student. From his own large experience, and from a wide reading of the literature on this subject, Dr. Niles has written an important contribution.

The Surgical Clinics of John B. Murphy, M. D., at Mercy Hospital, Chicago. Vol. I. No. 2. April, 1912. (*Philadelphia and London: W. B. Saunders Company, Published Bi-monthly.*)

With this publication and a series of papers appearing in the Journal of the American Medical Association the work of Dr. Murphy is securing very wide notice, and we regret that the Surgical Clinics are not better constructed. Were cases so grouped that deductions as to treatment, etc., in a variety of conditions might be correctly drawn, then these clinics would be of real service. But to read a number of case histories which have no close connection one with another, many of them reported but briefly, is a waste of time.

Tumors of the Jaws. By Charles L. Scudder, M. D. Illustrated. $6.00. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

Dr. Scudder in his preface states that there is no complete treatise on this subject in the English language, and his book, which is based in measure on the extensive records of the Massachusetts General Hospital, will prove most useful to the profession. It has been compiled with the author's well-known care and scholarship, and the statistics he has gathered and the cases he reports in brief make it especially valuable. "Tumors of the Jaws" is an important addition to surgical literature, and paves the way for other larger works on the subject or monographs on some of its special features. There are nine chapters on the following subjects: 1, epulis; 2, sarcoma of the jaws; 3, benign tumors of the jaws; 4, the odontomata; 5, carcinoma of the jaws; 6, the diagnosis and operative treatment of malignant disease of the upper and lower jaws; 7, tumors of the palate; 8, leontiasis ossea; and 9, prosthesis, followed by an index of names and index. The two longest chapters are those on sarcoma (100 pages) and odontomata (80 pages). The work is very abundantly illustrated, in this respect being the most remarkable collection of horrible pictures that we know of in any surgery. One of the blessings of modern surgery is the possibility of preventing persons ever becoming such monstrosities as are here portrayed. Many a surgeon and physician will turn away with loathing from these repellent pictures. The book is a gallery of horrors. The reproduction of these photographs may well be a question of taste and value, but it is impossible not to express our intense dislike of the selection of a frontispiece of the most hideous deformity of the human countenance in colors; elsewhere in the book it might have been tolerated, but to open on this is positively repulsive. As a piece of book-making, the publication is, we think, poor; heavy shiny paper, with very wide spacing between the lines of the text, and no use of different sizes of type to indicate the body of the text from case histories and statistics, thus making the volume much larger and heavier than necessary. The text is also so broken by the innumerable pictures as to make tedious reading. When will publishers cease to produce expensive works, which could be sold to many more readers were the price less? This is, for the doctor, one of the high costs of living.

Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India. By Major D. McCay, M. B., etc. Investigations into the Jail Dietaries of the United Provinces with Some Observations on the Influence of Dietary on the Physical Development and Well-Being of the People of the United Provinces. New Series. No. 48. Price 3/. (*Calcutta: Superintendent Government Printing, India, 1912*).

A short time since Major McCay, who is professor of physiology in the Medical College, Calcutta, prepared a similar report on the jail dietaries of Bengal, noticed in our issue of February, 1911. Such a report is of value to the Indian Government, but will find few readers except medical officers in India, and possibly some others interested in these physiological problems.

Epidemic Dropsy in Calcutta. Being the Final Report of an Enquiry Carried Out by Major E. D. W. Greig, M. D., etc. New Series. No. 49. Price 2/6.

The preliminary report was reviewed in our columns, January, 1912. The two papers make a valuable addition to our knowledge of this disease in an Eastern community.

Sprue: Its Diagnosis and Treatment. By Charles Begg, M. B., etc. Illustrated. (*New York: William Wood & Co.*)

Doctors who may go to the tropics to practice, and army and navy surgeons who at any moment may find themselves in these regions, will find helpful this new study of an obscure malady, for Dr. Begg writes after "over thirty years' clinical work in connection with this disease" (though he does not state where he has practiced). The author considers the geographical distribution, morbid anatomy, pathology, diagnosis and treatment of the disease, with additional chapters on cases, results in his last hundred consecutive chronic cases, and dysentery. He recommends strongly the use of *yellow* santonin, which he believes to be the most efficacious of all drugs in this disease. It must be left to other doctors to pursue this treatment further and determine its ultimate value. It is a brief monograph, which might have been easily, and with benefit, published in a volume of half the size of the present. Although stated to be illustrated it has only a few micro-photographic reproductions.

Report from Pathological Department and the Department of Clinical Psychiatry, Central Indiana Hospital for Insane. 1909-1910 and 1910-1911. Vol. IV. (*Indianapolis: Wm. B. Burford, 1912*).

We have noted before with satisfaction and pleasure the preceding volumes issued from this hospital, and are glad to again call attention to the work done in the above-named departments. Drs. Martin and Bahr, pathologist and psychiatrist, deserve much credit for the full reports from their divisions. They are adding valuable information along lines of work often neglected in insane hospitals, where the constant loss of material for scientific study is to be much regretted. The directors of many insane hospitals think that scientific workers in their institution are merely a needless expense, but it is gratifying to note that Dr. Edenharter, the superintendent of this hospital, recognizes how important such workers are to the welfare and fame of his institution, and that he has been able to obtain the means to support these men and has secured such active workers. With this start we are confident that these reports will win greater recognition in the future, and the State of Indiana is to be congratulated on the work done in this hospital. The appearance of the report, both in binding and printing, is exceptionally good.

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THE CUTANEOUS REACTION OF SYPHILIS.

PRELIMINARY NOTE.

By Julian Mast Wolfsohn, M. S., M. D.,
Medical House Officer, The Johns Hopkins Hospital.

Given a case of infectious disease, the first aim of the physician is to make an early and exact diagnosis. In order to do this, recourse to special methods, the difficulties and restrictions of which are beyond the reach of the general practitioner, is often necessary. The Wassermann reaction in syphilis is an instance in point. The desirability of more simple tests, which are at the same time accurate, is at once apparent.

Since the discovery of tuberculin by Koch, a new field in the diagnosis of tuberculosis has been opened. For diagnostic purposes many methods for the administration of tuberculin have been described, among which may be mentioned:

1. The subcutaneous method;
2. The cutaneous method of von Pirquet;
3. The ophthalmo reaction promulgated separately by Wolff-Eisner and by Calmette;
4. The percutaneous reaction of Moro and Goganoff; and
5. The intradermal method of Mantoux and Moussu. This last method, the authors state, is sufficiently sensitive to reveal tuberculosis in domestic animals. Administered in this way tuberculin gives rise to no general disturbance, and it is asserted that it possesses all of the advantages of the subcutaneous method for diagnosis and none of its disadvantages. This method is now being used widely for the diagnosis of human tuberculosis.

Other special diagnostic methods, such as that of complement fixation and that of the opsonic index have been recommended from time to time, but the results have been extremely variable; they seem to be of little value.

Undoubtedly, through the use of tuberculin, great strides have been made in the early diagnosis of tuberculosis, but to devise the methods the causative organism had first to be isolated and cultivated.

Shortly after the results of the tuberculin tests were reported, many workers, including Wolff-Eisner, Didrachi, Neisser, Bruck, and others, attempted, by applying extracts of syphilitic tissues to the skin of syphilitic patients to obtain a specific reaction. The results were discordant. Neisser and Bruck asserted that the method was valueless, inasmuch as a reaction similar to that produced by the syphilitic extract also could be obtained by the employment of a concentrated extract of normal liver.

Fontana,[1] in a comprehensive report, showed the apparent lack of uniformity in results obtained by various authors. He went over the same ground as these authors, controlling the results by Wassermann reactions. He used several other substances which would lend themselves to intradermal reaction in syphilitic subjects, and compared the results with control tests in the non-syphilitic, as for example:

1. Syphilin, which is a glycerine extract of mucous patches, rich in spirochætes;
2. 10% solution of sodium glycocollate in sterile, distilled water.

[1] Dermat. Wchnschr., 1912, No. 3, 119.

3. Lecithin in the form of phosphoplasmin; and
4. Extract of normal guinea-pig's heart.

A positive reaction was indicated by a distinct nodular infiltration. It is interesting to note that of forty syphilitics, 85% showed positive Wassermann reactions, and only 45% developed positive syphilin reactions. Of sixteen non-syphilitics, 12½% gave positive tests. The results did not seem to be influenced by antiluetic treatment.

Using the sodium glycocollate solution in twenty-nine syphilitics he obtained a positive reaction in only 40%, and in fifteen non-syphilitics a negative reaction in all. In twenty-two syphilitics, in which both the Wassermann reaction and the intradermic tests with glycocollate solution were made, 89% showed positive Wassermann reactions, and 27% positive glycocollate solution reactions.

Lecithin injections produced only three positive tests in eighteen luetic cases.

Extract of guinea-pig's heart was used in three patients suffering from syphilis, all of whom gave positive reactions, whereas of ten non-syphilitics only two reacted positively.

The author's conclusions, drawn from this series are, that, "of these substances, syphilin *may* become of some use in the future." Neisser and Bruck early found that the skin of syphilitics late in the disease is in a state of *Umstimmung,* or susceptibility to trauma, and this may readily explain the reaction to the injections of extract of guinea-pig's heart in the skin of syphilitic subjects.

In 1905, Schaudinn established the spirochæte pallida as the causative agent for syphilis. Numerous efforts were made to isolate the organism in culture, but without success. It remained for Noguchi[2] to discover the method of cultivating these organisms, first by the indirect, later by the direct method. He showed that in order to cultivate the pallida directly from the primary lesions in man, two all-important conditions must be fulfilled:

1. The maintenance of strict anærobiosis; and
2. The property possessed by the spirochætes pallida of migrating in solid media in which they are multiplying.

The culture media used consists of:

1. Ascitic fluid containing a piece of sterile placenta; and
2. Ascitic fluid agar, also containing a piece of placenta.

The organisms are grown for 6 to 50 days. After sufficient growth has taken place the tissue is removed, and the solid media and organisms ground in a mortar and diluted with the ascitic fluid culture. The mixture is then heated for 60 minutes at 60° C., and 1% tricresol is added as an antiseptic. Noguchi has called this final sterile emulsion "luetin," and it is this preparation which was used in the tests reported in this paper.

As Noguchi l.c. points out "pure cultures of the treponema pallida offer many advantages, because not only are pallida of different ages present, but also their metabolic products," which, he states, are important factors in establishing an allergic state in syphilitic subjects.

[2] J. Exp. M., 1911, xiv, 99. Idem. 1911, xiv, 556.

Method.

In the following series of cases the method advised by Noguchi has been strictly followed.

Both arms of the patient were cleaned with 95% alcohol; 0.1 cm. of the luetin was injected intradermally into the left arm over the biceps muscle and the same amount of the control emulsion (which consists of the media only and no pallida) was similarly injected into a corresponding site on the right arm.[3] Observations were made daily thereafter over a period of twelve to thirty-six days.

To insure the sterility of the emulsions, cultures from them were frequently made.

Every patient upon whom the luetin test was tried, had a Wassermann reaction done on his blood serum and upon his cerebrospinal fluid, when this was indicated.

Very few reactions presented any difficulty in interpretation, i. e., practically all the reactions were definitely negative or positive.

The Negative Reaction.

In the majority of cases, 24 hours after the injection, the skin in the injected arm showed a slight blush, and a moderate induration or papule formation. Very seldom was any tenderness or itching complained of, which has been only too frequent in the cases showing positive reactions.

Almost invariably, after 48 hours, the injected site would be free from induration and erythema; a pinpoint ecchymosis or perhaps a small yellowish pigmentation alone remained. If the patient has irritated the site of injection a small pustule may form, but this latter has only developed in two of the control cases and has not given rise to confusion in interpretation.

Positive Reaction.

Though the type of reaction in positive cases varies greatly, in general the gross characteristics are induration and erythema. In analysing the various types of reaction found in the different stages of syphilis, the following classification includes all the essential varieties:

(a) *The Papular Form.*—Arising at the site of the injection within 24 hours an indurated papule developes which varies in size from 5 to 15 mm. in diameter and this is surrounded by more or less erythema and is usually quite tender. The reaction gradually increases in size until the 3d or 4th day, when it either regresses or developes into the pustular form. The control injection (in the other arm) in these cases usually shows no reaction after 24 to 48 hours.

(b) *Vesicular Form.*—This variety is generally seen in cases where a moderate reaction rapidly follows the injection, and it occasionally appears as a bleb, but more often as a group of small vesicles superimposed on an indurated, tender base. As a rule, the vesicular passes into the pustular variety.

[3] To correctly perform the intradermic injection, the hypodermic needle, which must be of very fine bore (e. g., the Sub Q syringe needle) is inserted almost parallel to the skin in an effort to reach the under surface of the derma. The bevel on the end of the needle should be turned toward the skin.

(c) *Pustular Form.*—This may be primary or secondary. When primary it occurs usually in association with the violent reactions seen in latent or in late tertiary stages of syphilis where no treatment had been previously administered. When secondary it occurs late in the papular form or developes early from the vesicular stage.

The pustules usually rupture spontaneously with subsequent crust formation.

In a few latent and parasyphilitic cases a week after all evidence of reaction at the site of the injection had subsided a hemorrhagic pustule appeared, which, when opened, exuded a semi-fluid grumous hemorrhagic material.

(d) *Torpid Form.*—Noguchi has aptly so named this variety. It was found that, in many of the parasyphilitics showing vascular luetic lesions, for 3 to 7 and even 28 days following the injections, the reactions were quite negative; but the site of injection, after this period of quiescence, possesses a bluish-red tinge and a smaller or larger indurated papule is felt. This soon increases in size, is not tender, and in the 2 or 3 days following developes into a pustule, after which there is a regression of the reaction. In these cases the control injection site showed nothing abnormal.

In brief, the reactions may be said to be (1) mild, (2) violent, or (3) torpid, according as the signs slowly develop to a maximum and regress; start in violently reaching an early maximum, which is maintained for 24 to 72 hours, and then subsides; or develop late and show only a mild reaction after a latent period and never become marked.

In no case did scar formation follow after local manifestations subsided, but in many instances there was more or less pigmentation, according as the site of injection was markedly hemorrhagic or not.

Non-Syphilitic Cases.

Of the seventy controls in which the patients were suffering from diseases other than syphilis, e. g., soft chancre, mitral insufficiency, myocardial insufficiency, cancer of the tonsil, acute rheumatic fever, pregnancy with still born infant, senile palsy, bronchitis, brain tumor, diabetes mellitus, pleurisy with effusion, pericarditis, hypophysis tumor, pernicious anæmia, epilepsy, peliosis rheumatica, sarcoma of the ileum, myelogenous leukemia, carcinoma of the stomach, thyroid cyst, pulmonary tuberculosis, chronic nephritis, rickets, chronic constipation, gastric ulcer, uræmia, typhoid fever, and infectious arthritis, etc., when no history of syphilitic infection could be obtained and where the Wassermann reaction was negative in each case, no positive luetin or control reactions were obtained. In two cases, small non-indurated pustules developed within three days after the injection, but these easily could be distinguished from the positive reactions. No constitutional symptoms were complained of or noted in these cases.

Primary Syphilis.

No opportunity as yet has been afforded to try this test on patients suffering from primary syphilis.

Secondary Syphilis.

Two cases of secondary syphilis, both in the maculo-papular stage, were inoculated. In each case the Wassermann reaction was positive and each patient had been given 0.4 gram salvarsan intravenously 24 to 48 hours before the test was given. Both tests were positive. In the first case the salvarsan had been administered only 24 hours before, but the reaction to the luetin, although delayed till the fifth day, was definitely positive. No constitutional symptoms or reaction (*Umstimmung*) over the site of injection of the control emulsion were noted.

Tertiary Syphilis.

This series includes six cases in which the Wassermann reaction was positive in five. The sixth patient had had 0.6 gram of salversan one year before admission and his test proved negative both with blood serum and cerebrospinal fluid at this time. The Wassermann reaction was positive in 1911, however. The luetin reaction in this case was positive. In the first case of this series the luetin reaction was negative though the Wassermann was positive. This case was not followed longer than 10 days.

The reaction in four cases of luetic periostitis was of the violent variety and showed early pustule formation and rather marked reaction on the control side (*Umstimmung*). Two of these complained of tender and painful arms and one developed enlargement of the axillary glands. All these manifestations disappeared in 48 hours.

It is interesting to note that, in one case, two weeks after subsidence of the local manifestations there was a flare up at the site of the injection of luetin. A pustule formed and rapidly disappeared, leaving no other signs than slight desquamation and pigmentation.

The rapidity with which the reaction becomes manifest, the ease with which it is interpreted, together with the almost constant development of it, in this stage of the disease makes it a most valuable aid in diagnosis. It not only checks up the Wassermann reaction, but it may be indeed supplementary to it, especially in the treated cases, in which the Wassermann reaction not infrequently may be negative.

Parasyphilis.

If one accepts the newer conception of parasyphilis he will include not only tabes and general paresis, but also those cases which show vascular changes of luetic origin, e. g., cases of syphilitic mesaortitis and aortic aneurysms. Therefore, included in this series are nineteen cases, seven of which are of central nervous system affection, and twelve of cardiovascular disturbance.

A careful analysis of these cases shows the great value of the luetin test. Of the former cases all seven gave positive tests, while the Wassermann test was negative in six.[4] One of

[4] Of course one must keep in mind the limited number of cases that the luetin test has been tried on; the result, however, even in this small series has been striking.

these, a tabetic, had a positive Wassermann reaction one year previously and had had in the interim three doses of salvarsan, but the cerebrospinal fluid still gave a positive Wassermann test. The luetin reaction in this case was violent, the reaction over the site of control injection (*Umstimmung*) being especially noticeable, as it was also in five of these cases.

Another tabetic who showed no other signs than diminished knee kicks and sluggish pupils, developed remarkable constitutional symptoms, beginning 30 hours after inoculation and lasting four days. These symptoms consisted of fever as high as 103° F., pain in the abdomen resembling crises, with nausea and vomiting. The reaction was violent and *Umstimmung* was present. The Wassermann reaction was negative, both for the blood serum and cerebrospinal fluid in this case. This patient had never received treatment previous to this time.

Of the twelve parasyphilitics showing cardiovascular lesions, eleven gave positive luetin reactions and one reacted negatively. Only seven showed positive Wassermann reactions. The one case giving a negative luetin test had a positive Wassermann reaction. But six of this series giving negative Wassermann reactions gave positive luetin tests. It is in this group of cases in which great care must be exercised, as one might readily consider the test negative if it were not watched for some time. Six of these twelve cases showed reactions of the torpid form, no sign of the reaction appearing until the 9th day, and in one case of abdominal aneurysm, which gave a positive Wassermann test, there was no manifestation until the 28th day. The luetin reaction will prove of great value in this type of case, if properly followed, because the Wassermann tests are relatively inconstant. *Umstimmung* is infrequent here as compared with cases of parasyphilis of the central nervous system. No other cases showing constitutional symptoms were noted.

Latent Syphilis.

This stage of syphilis shows a wonderful constancy of results with this test. In the twenty-three cases of latent syphilis tested all gave positive reactions. The Wassermann reaction in this series was positive only in ten cases. In three of these cases the Wassermann reaction with the cerebrospinal fluid was also negative.

Some of the cases reported in this group denied having contracted syphilis, but after the luetin test was found positive, in several instances the patients confessed having had a primary lesion or secondary manifestations. The test was applied in four cases of pregnancy, three of which were terminated by the birth of mascerated fœtuses and the fourth by the birth at term of a still born infant. All four patients denied infection. The three former patients reacted "violently" to the luetin and showed *Umstimmung*. The Wassermann reaction was positive and an anatomical diagnosis of syphilis in the infant was made in each case. The fourth case gave a negative luetin reaction, the Wassermann reaction was negative and no signs of syphilis could be discovered in the dead infant. No constitutional disturbances were noted in these cases.

Of the remaining nineteen cases in this series, nine showed *Umstimmung*. One patient suffering from carcinoma of the head of the pancreas, who had a chancre in 1865, showed a delayed luetin test, but gave a negative Wassermann reaction.

Constitutional Symptoms.

Constitutional symptoms consisting of tender axillary glands, tender arms, tachycardia, abdominal pains, bone pains and nausea were present in four of the cases, but these symptoms were usually of only 24 to 48 hours duration and caused no alarming discomfort to the patient. One case showed a secondary hemorrhagic pustule two weeks after the first manifestation had subsided.

Thus, latent syphilis, so difficult to diagnose clinically and in which the Wassermann reaction is not of assistance in over 40% to 70% of the cases, shows a positive luetin reaction in all the cases tried. It seems that the luetin reaction will prove of even greater value in the diagnosis of this group than in the tertiary stage in which the Wassermann reaction is more constantly present. The effects of treatment on the results of the luetin test in latent syphilis has not been significant.

Umstimmung.

In reviewing the whole series of one hundred and fifty cases, another interesting fact was noted—that in many cases of tertiary and of latent syphilis the site of the control injection showed almost as marked a reaction as developed about the point where the luetin was injected. This, as was pointed out by Neisser and Bruck, and which seems to be confirmed by Noguchi and this series of tests, appears to be due to the susceptibility to trauma of the skin of syphilitics late in the disease (*Umstimmung*), for not one of the seventy control patients reacted on the side in which the control emulsion was injected. (Experiments are now under way in which a series of patients, not selected, are being inoculated with the control emulsions only.)

The cases exhibiting the most marked "control" reactions (*Umstimmung*) were those suffering from syphilis in its later stages. The inconstancy of this phenomenon in all probability precludes its being of an allergic nature, which, Noguchi, I believe, has so well shown the principle of the luetin reaction to be.

Conclusions.

1. The luetin reaction is specific for syphilis.
2. The reaction is found of greatest value in the latent and tertiary stages of the disease.
3. In some treated cases of secondary syphilis the reaction is positive.
4. In parasyphilitics with the cardiovascular manifestations of the disease the reaction may be delayed for from 9 to 30 days.
5. The luetin reaction is helpful in the diagnosis of latent syphilis in pregnancy.
6. The state of *Umstimmung* is well brought out in the tertiary and latent forms of syphilis.

SECONDARY SYPHILIS.*

Diagnosis.	Treatment.	Luetin.						Remarks.	Luetin React.	Wassermann.	Constitutional.
			First day.	Second day.	Third day.	Fourth day.	Later.				
Secondary Syphilis (maculo-papular)	"606" 24 hrs. before luetin test given	Lu.	Papule with wide eryth.	Papule; little eryth.	Regression	Eryth. for 1 cm.	Pustule, scab and eryth. in 5, 6, and 7 days	Reaction delayed to 5th day	+	+	Temp. 99.8° F.
		Co.	Small vesicle	No react.	No react.	No react.	No react.				
Secondary syphilis	"606" given 48 hrs. before luetin test	Lu.	Induration and eryth. for 1 cm. *Vesicles*	Many small pustules, eryth. 2½ cm.	Larger erythema, pustules	Large pustules	Pustule ruptured 7th day				
		Co.	Small red nodule	Nodule	.....	.....	.....	.....	+	+	
									2	2	

TERTIARY SYPHILIS.

Diagnosis.	Previous treatment.	Luetin.						Remarks.	Luetin React.	Wassermann reaction. Blood C. S. F.	Constitutional.
			First day.	Second day.	Third day.	Fourth day.	Later.				
Syphilitic cirrhosis of liver; Pulm. tuberculosis.	1896-1899 long irreg. intervals	Lu.	Small nodule	.....	.....	.....	No reaction; slight pigmentation left	.....	Negative	+ Not done	
		Con.	Same								
Syphilitic periostitis	3 months; chancre, secondaries	Lu.	Large indurated papule 5 cm.	Same	Large raised pustule; scab, eryth. regressing	Regression	Flare up 2 wks. later	2 wks. after subsidence of flare up on luetin site pustule *Umstimmung*	+	+ Not done	Enlarged axillary glands
		Con.	Papule and eryth. for 3 cm.	Same	Regression	Scab					
Syphilitic periostitis	None (no hist.)	Lu.	Induration 1 cm.; eryth.	Pustule and eryth. 1.5 cm.	Pustule broke; eryth.	Regression	.....	Pustule *Umstimmung*	+	+ Not done	
		Con.	Same	Large raised papule	Papule and eryth.	Regression					
Syphilitic periostitis *Gummata*	None (no hist.)	Lu.	Vesicles 1 cm.; eryth. slight.	Large irreg. pustule 1.5 cm.	Same	Pustule broke; scab regression.	Regression	Vesicle pustule *Umstimmung*			
		Con.	Small papule	Induration 1 cm.	Pustule formation	Smaller	Regression	.....	++	+ Not done	
Hemiplegia arterio-sclerosis	"606" 1 yr. previously. No hist.	Lu.	Indurated patch	Induration 1½ cm.	Increasing to 2 cm.	Increasing small pustule.	Regression	.....	+		
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction				
Luetic periostitis; polyarthritis	None (no hist.) Miscarriage	Lu.	Induration and diffuse eryth.	Large pustule; eryth. 2.5 cm.	Same	Regression	.....	Pustule	+	+ Not done	Tender arm
		Con.	Small indurated papule	Pustule and eryth. 1.5 cm.	Same	Regression	.....	*Umstimmung*: violent react.	++		
									5 positive 1 negative	5 positive 1 negative	

PARASYPHILIS.

Cerebro-spinal syphilis; beginning dementia paralytica	3 *days*; chancre 1899; iritis 1899	Lu.	Papule and eryth. 2 cm. tender	Pustule; eryth. 3 cm.	Same	Pustule broke	Regression	No scar; on 12th day either side pustule	+	+ +	Tachycardia to 110
		Con.	Papule; slight eryth.	Pustule and eryth.	Pustule same size on left	Same	Regression	*Umstimmung* rapid			
Myocardial insufficiency; aortic insuff.; syphilis (Wass.)	3 weeks; chancre 1887	Lu.	Induration and eryth. 1 cm.	Very slight infiltration	No reaction	No reaction	No reaction	.....	..	+ Not done	
		Con.	No reaction	No reaction							
Transverse myelitis	3-4 months; chancre 1902; secondaries	Lu.	Papule and eryth. 7 mm.	Same	Same	Pustule and infiltration 1.5 cm.	Pustule broke 9th day	.....	+	.. Not done	
		Con.	No reaction	Same	No reaction	No reaction	No reaction				

* In all tables the abreviations indicate as follows:
Lu. = luetin. Con. = control. Eryth. = erythema. C. S. = cerebro-spinal. Wass. = Wassermann. C. S. F. = cerebro-spinal fluid

PARASYPHILIS—*Continued.*

Diagnosis.	Previous treatment.	Luetin.						Remarks.	Luetin React.	Wassermann reaction. Blood C. S. F.		Constitutional.
			First day.	Second day.	Third day.	Fourth day	Later					
Myocardial insuff.; aortic insuff.	None; secondaries 1911	Lu.	Pustular induration 1½ cm.	Increased reaction	Regression	Regression	Reaction ended	.....	+	..	Not done	
		Con.	Slight eryth. 1 cm.	Same	No reaction	No reaction	No reaction					
Aneurysm aortic arch	None; chancre 1908	Lu.	Small papule	No reaction	No reaction	No reaction	On 11th day area inflam.	Delayed pustule	+	..	Not done	
		Con.	Same	No reaction	No reaction	No reaction						
Myocardial and aortic insuff.	None (no history)	Lu.	Large induration and eryth.	Same	Regression; some eryth. still.	Small pustule broke 6th day	.....	.....	+	..	Not done	
		Con.	Small papule	No reaction	No reaction	No reaction						
Myocardial insuff.	None (no history)	Lu.	Indurated papule; eryth.	2 small vesicles; induration.	2 pustules; eryth. 1 cm.	Same	Vesicles again on 7th day	2 crops of vesicles; pustules	+	20% fixation	Not done	
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction					
Myocardial insuff.	None (no history)	Lu.	Indurated papule 1 cm.	Increased induration and eryth.	Small pustule; induration; same	Went home	Went home	.....	+	+	..	
		Con.	Same	Smaller papule	Regression							
Aortic insuff.	1 year; chancre 1899; secondaries 1899	Lu.	Slight indurated papule and eryth.	Same	No reaction	No reaction	On 9th day much induration and eryth. 2 cm.	Delayed	+	..	Not done	
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction					
Dementia paralytica C. S. Lues	Short while? chancre	Lu.	Induration and eryth.	Induration and eryth. for 2 cm.	Larger induration; pustule	Pustule broke; crust; regression	Regression	Vesicles and pustules; *Umstimmung*	+	..	..	
		Con.	Papule	2 small vesicles; induration	Large infiltration	Pustule	Regression					
Aneurysm of aortic arch; myocardial insuff.; syphilis (Wass.)	None	Lu.	Nodule small	Regression	Regression	Regression	3 weeks later flare up in control; *hemorrhagic*	Delayed *reaction.* 3 weeks' hemorrhagic in luetin side	+	+	Not done	None
		Con.	Nodule small	Regression	Regression	Regression						
Aneurysm of abdominal aorta; syphilis (Wass.)	3 mos. (1890) (primary and secondaries)	Lu.	Nodule small	Regression	Regression	Regression	4 weeks after luetin inj. =eryth. some infiltration *pustule*	*Delayed*	+	+	Not done	None
		Con.	Nodule small	Regression	Regression	Regression		Pustular				
Tabes dorsalis; acromegaly; syphilis (Wass.)	1 mo. 1897; 3 doses "606" 1911-1912; prim. and secondaries	Lu.	Infiltration and eryth. 3 cm.	Vesicles and induration	Large indurated mass with eryth.	Regression	6th day react. over; pigmentat. desquama	*Rapid* react.; vesicles; pustules; both sides react. con. more than luetin	++	+1911 —1912	+1912	None
		Con.	Eryth. and induration 1.5 cm.	Regression	Larger induration pustules	Regression	Same; no scar		+++			
Arterio-sclerosis; aortic insuff.; syphilis (Wass.)	3-4 weeks 1900; prim. and secondaries	Lu.	Induration red area 7 mm.	Increasing area of induration 1.5 cm,	Pustule	Regression scab	No further reaction	Rapid react.	+	+	Not done	None
		Con.	Same as Lu.	Small papule	Less reaction	Small pustule; no induration; no eryth.	Regression					
Myocardial insuff.; aortic insuff.; syphilis (Wass.)	1 week (1899) chancre	Lu.	Small infiltrated papule 5 mm.	Same	Small desquamation; papule	Regression	14th day 2d pustule	*Delayed*	+	+	Not done	None
		Con.	Infiltrated papule 4 mm.	No reaction	No reaction	No reaction	No reaction	Pustule				
Myelitis	None	Lu.	Indurated papule with tenderness 1.5 cm.; eryth.	Small pustule; some induration	Increasing induration and pustule	Same	Pustule broke 6th day	Both sides reacted; control delayed; pustules; *Umstimmung*	+	..	Not done	None
		Con.	Same; less eryth.	Same at 28 hrs.	Small pustule	Fluctuating pustule	Scab					
Tabes dorsalis; chr. nephritis	3 mos. (1897) chancre	Lu.	Large red papule 8 mm.	Small tender pustule; induration for 1.2 cm.	Scab; induration	Regression	4 weeks later 2d induration and pustule foll.	2d *delayed* react. in luetin side	+	+	..	None
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction	*Pustule* formation				

PARASYPHILIS—*Continued.*

Diagnosis.	Previous treatment.	Luetin.						Remarks.	Luetin React.	Wassermann reaction. Blood C. S. F.		Constitutional.
			First day.	Second day.	Third day.	Fourth day.	Later.					
Aneurysm of aortic arch	1 year: chancre 1892	Lu.	Small indurated papule	Small pustule; induration still present.	Same	Small blood crust; less induration	Regression	Mild react.; *pustule*	+	+	Not done	None
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction					
Tabes dorsalis	None (no history)	Lu.	Slight induration; diffuse eryth.	Induration; eryth. for 3 cm. pustule	Large pustule with crusts; eryth. 3 cm.	Samo	Regression	Rapidly fulminating case; *pustule* formation	+	..	..	Fever to 103°F. pain in abdomen; vomiting and nausea beginning 30 hrs. after and lasting 4 days
		Con.	No reaction	Slight induration	Small pustule; little reaction	Same	Regression	*Umstimmung*				
									18 positive 1 negative	10 positive 8 negative 1 C. S. F. positive		

LATENT SYPHILIS.

Acute lobar pneumonia	2 months (chancre 1909)	Lu.	No induration; slight blush.	Indurated papule	Small pustule; eryth. 6 mm.	Large pustule	Not seen	.....	+	..	Not done	
		Con.	Same	No reaction	No reaction	No reaction						
Typhoid fever (?)	1-2 days; secondaries 1900	Lu.	Large eryth. 6 cm.; induration 2 cm.	Few vesicles added	Large infiltrated pustules with erythema.	Confluent pustules	8th day pustule broke	Violent reaction; hemorrhagic after 2 wks.	++	..	..	Very tender axillary glands 2 weeks
		Con.	Induration and eryth. for 2 cm.	25 small pustules	Regression	Regressing	No reaction	Pustules. *Umstimmung*				
Pulmonary tuberculosis?	1 year constantly (chancre 1911)	Lu.	Induration and eryth.	Large pustules	Pustule broke	Regression	No reaction	Pustule. *Umstimmung*	+	..	Not done	
		Con.	Eryth. 2 cm.	Papule with erythema	Small pustule	Regression	No reaction					
Subacute appendicitis	None (no history)	Lu.	Induration and eryth. for 1 cm.	Several small vesicles with eryth.	Large pustule; eryth. 8 cm.	Pustule broke	Scab	Vesicles pustule	+	..	Not done	
		Con.	Same	Papule	Large papule	Pustule	Regression	*Umstimmung*				
Aortic insufficiency	None (no history)	Lu.	Large induration and eryth.	Same—2 cm.	Same	Regression	Small pustule	.....	+	..	Not done	
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction					
Pregnancy syphilis (Wass.)	None (macerated fœtus)	Lu.	Induration and eryth. 2.5 cm.	Eryth. and few large vesicles.	Regression	Not seen	Not seen	Vesicles; violent reaction	++	+	Not done	
		Con.	Small hard papule	Slight papule	No reaction							
Brain tumor (?) hysteria	6 mos. (chancre 1895)	Lu.	Induration, vesicles, eryth. 3 cm.	Pustules, eryth. and induration 4 cm.	Same	Regressing	Regressing	Vesicles; pustules	++	..	..	
		Con.	Induration and eryth. 1 cm.	Same	Large button	Regressing	Regressing	*Umstimmung*				
Latent syphilis; "basilar meningitis"	"606" 1911 (chancre 1873)	Lu.	Many small pustules; eryth. 4 cm. induration.	Same	Same	Regressing	React. over 9 days	Pustules *Umstimmung*	+	..	Not done	
		Con.	Pustules and eryth. 3 cm.	Large indurated button	Same	Regressing						
Hysteria (?)	None (no history)	Lu.	Papule with eryth. for 2 cm.	Same	Eryth. and induration persists.	Small pustule broke	Regression	.....	+	..	Not done	
		Con.	Small papule	No reaction	No reaction	No reaction	No reaction					
Rheumatic fever; syphilis (Wass.)	None (no history)	Lu.	Infiltrated button	Infiltration with eryth. 1.2 cm.	Same	Pustule	5-6 days; larger pustule	7th day slight desquamation; nodules more tender; pustules: reaction in both sites; *Umstimmung*	+	..	Not done	Nodules were very tender
		Con.	Smaller button	Small vesicle	Small pustule crust	Regression	Reaction over					

LATENT SYPHILIS—*Continued.*

Diagnosis.	Previous treatment	Luetin.						Remarks.	Luetin React.	Wassermann reaction. Blood C. S. F.		Constitutional.
			First day.	Second day	Third day.	Fourth day.	Later.					
Chronic nephritis	None (no history)	Lu.	Small indurated erythema	Larger nodule; eryth.	Small pustules	Not followed further	.....	Pt. showed signs of old choridoretinitis both eyes	+	..	Not done	None
		Con.	Small nodule	No reaction	No reaction							
Splenic anæmia	None (chancre 1904) (cauterized)	Lu.	Indurated eryth. area 2.5 cm.	Large tender induration; pustule	Pustule broke; scab	Local react. gone	Reaction over 9th day	Pustule *Umstimmung*; rapid reaction	+	..	..	Tachycardia to 100; abdominal pain over enlarged spleen
		Con.	Small indurated area	Papule with eryth.	Large pustule; eryth.	Pustule broke	Reaction disappeared 11th day					
Post. urethritis; tuberculosis. syphilis (Wass.)	None (no history)	Lu.	Small tender papule	2 small vesicles	Same	Small pustule	10th day 2d pustule and induration	2d induration; pustule	+	+	Not done	None
		Con.	Same	Papule with eryth.	Same	No reaction	No reaction					
Catarrhal jaundice syphilis (Wass.)	None (no history)	Lu.	Induration and eryth. 1 cm.; vesicle.	Pustule with eryth. 1.5 cm.	Pustule and eryth. 2.5 cm.	Increasing induration	Regression	.....	+	+	Not done	None
		Con.	Papule and eryth.	Papule and eryth. 1 cm.	Pustule and eryth. 1 cm.	Many small pustules	Regression					
Hysteria; syphilis (Wass.)	1 year at intervals	Lu.	Induration and eryth. 4 cm.	Vesicular and pustular formation	Same	Regression	12th day all signs gone	Pustule *Umstimmung*	+	+	Not done	Bone pains and nausea 12 hrs. after injection; temp. 99.8° F.
		Con.	Blush 2 cm.	Eryth. 2 cm.	Induration and eryth.	Pustule	Same					
Acute bronchitis; syphilis (Wass.)	None (no history)	Lu.	Induration and eryth. 5 cm.	Induration 7 mm.	Induration 1 cm.	Crust; no induration	Nothing 5th day	.....	+	+	Not done	
		Con.	Small papules	Small eryth. papule	No reaction	No reaction	No reaction					
Pulm. tuberculosis; syphilis (?)	None; no history (patient has old iritis)	Lu.	Induration and eryth. for 2 cm.	Same	Same	Small pustule with eryth. 1.5 cm.	Pustule broke 7th day	Pustule	+	..	Not done	
		Con.	Small papule	Small eryth. papule	Regression	Regression	No reaction 5th day					
Carcinoma of head of pancreas	None; chancre 1872	Lu.	Small papule	Same	Regression	Increasing	7th day induration 1 cm. pustule 10th day larger.	Delayed hemorrhagic and luetin after pustule	+	..	Not done	
		Con.	Small papule	Same	No reaction	No reaction	No reaction					
Paroxysmal tachycardia; syphilis (Wass.)	None (no history)	Lu.	No induration; eryth. 1 cm.	2 small papules; little eryth.	10 small pustules with eryth.	Pustules coalesced	Regression	.....	+	+	Not done	
		Con.	No reaction	No reaction	No reaction	No reaction	No reaction					
Pregnancy; syphilis (Wass.)	None (macerated fœtus)	Lu.	Induration and eryth. 2.5 cm.	Induration and large pustules.	Larger induration and eryth.	Not followed	.....	Vesicle; pustule; *Umstimmung*	++	+	Not done	
		Con.	Same	Very large button with vesicle	Regression							
Pregnancy; child; syphilis (Wass.)	None (macerated fœtus)	Lu.	Induration and eryth. 2.5 cm.	Increased induration and eryth.	Induration and eryth. for 3 cm.	Not followed	.....	*Umstimmung*	++	..	Not done	
		Con.	More induration than luetin side	Larger reaction	Large button							
Hemiplegia	No history; no treatment	Lu.	Induration and eryth. 1 cm.	Large. red, indurated papule 1 cm.	Same	Same; slight regression	Regression	*Umstimmung*	+	..	Not done	
		Con.	Small infiltrated papule	Same	Same	Regressing	Regression					
Carcinoma of jaw	Treatment 1 mo. for 10 yrs. (chancre 1902)	Lu.	Indurated papule; little eryth.	Same	Small hard papule	Same	Small crust 6th day	.....	+	+	Not done	
		Con.	Slight papule	No reaction	No reaction	No reaction	No reaction					

STUDIES IN TUBERCULOSIS.*

By Gerald B. Webb, M. D., Colorado Springs, Colo.

Vaccination.

It gives me unusual pleasure to relate to you to-night the investigations we have been making in the West in tuberculosis, for most of the laboratory work has been carried out by two of your own men, Dr. William Whitridge Williams and Dr. George Burton Gilbert, and I am most grateful to them for their assistance.

In spite of improved hygienic conditions every individual is exposed at some time to virulent tubercle bacilli. Hygiene, whenever tried alone without vaccination, has always failed to stop small-pox, and Professor Karl Pearson [1] has recently written, in summarizing the results gained by hygiene and education against tuberculosis, "The relative number of deaths from phthisis has not been diminished by the campaign against the tubercle bacillus, although the absolute number has fallen, but at a sensibly retarded rate."† By means of the skin tuberculin tests it has been shown that in many communities almost every child by the age of puberty has become infected. The present interpretation of this infection allows us to consider that it is nature's crude method of vaccination; the child which survives is placed in a hypersusceptible condition in regard to the tubercle bacillus; the organism possesses now the power of safe defence against small numbers of tubercle bacilli, yet against large numbers the infected organism is more helpless than the non-infected. The condition is one similar to anaphylaxis.

This infection may remain during the whole life of the individual—it would seem to be kept in better abeyence during childhood—but at any time it may lead to destruction of the host through escape of large numbers of bacilli from within, as well as from new massive infection from without.

That in spite of all care generations will continue to become infected would seem to be assured by the recognition of the small numbers of bacilli necessary to cause infection. We have ascertained that from virulent cultures inoculated subcutaneously twenty-five bacilli of the human type infected a guinea pig, seventy-five bacilli of bovine type infected a rabbit, and one thousand infected a calf. We have not yet determined the exact number of human tubercle bacilli that will infect a Rhesus monkey, yet the work we have done would indicate that a few hundred would suffice, and we may presume that children become infected by a similar small number.

Since civilization necessitates this exposure to living tubercle bacilli, the numbers and virulence of which cannot be controlled, and also since these bacteria attack especially vulnerable tissues with the unsatisfactory condition of infection just described, the question at once arises whether, if we could control the numbers, virulence, and point of attack before Nature infects us, we might not possess a form of vaccination which should protect us.

Attempts at the production of immunity to tuberculosis by means of inoculation of dead tubercle bacilli or their products have so far not on the whole been satisfactory. This failure may perhaps be explained in several ways.

The inoculation of the bacillary products may have resulted in an anaphylactic condition of the animal experimented upon, or the subsequent tests for immunity may have been made with too overwhelming numbers of living tubercle bacilli.

The most recent work in this country in the attempt to produce immunity by means of dead products of tubercle bacilli is that of Krause [2] of Saranac (N. Y.) and Meakins [3] of Montreal (Can.). By the use of a watery extract Krause found that the more frequently he inoculated the more hypersensitive the guinea pigs became. In testing the immunity by a subsequent inoculation of a small dose of living tubercle bacilli he found that in general the more protein the animal received during preliminary treatment the less the resultant infection.

Meakins used inoculations of an emulsion of dead tubercle bacilli and found that if given in sufficient amounts over a long enough period he produced an active immunity to virulent tubercle bacilli. He found these inoculations increased very markedly the phagocytic power of the blood. He suggests that the injection of killed tubercle bacilli might be taken advantage of to produce an immunity in infants before they become primarily infected with tuberculosis. The question at once arises in considering this dosage of tuberculo-protein whether the animals do not become hypersensitive.

I am somewhat inclined to believe with Koch that in the production of immunity to tuberculosis "We shall never obtain better results with non-living bacilli."

It was natural that the application of the living tubercle virus for the production of immunity should have been attempted in cattle. The results, however, of the inoculations of living human tubercle bacilli for the production of bovine immunity have not proven satisfactory. This failure may probably be in part ascribed to the fact that the cattle become hypersensitive, as for some time after the inoculations they may react to tuberculin; in other words true immunity has not been evoked.

In the recently published volume of the Bureau of Animal Industry the following conclusions are reached by the investigators Schroeder, Cotton, Mohler and Washburn:

"Though results have been obtained which are very encouraging to the investigators and which prompt them to strive onward with renewed vigor and hope, no system of bovovaccination has reached a stage at the present time that justifies its use in common practice."

The recorded experiments of the British Royal Commission on tuberculosis go to prove the importance of dosage in the transmission of tuberculosis.

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* Paper read at a meeting of The Lænnec, a society for the study of tuberculosis, The Johns Hopkins Hospital, March 25, 1912.

† This is probably not so true of New York City where more active preventive measures have been adopted, resulting in a more rapid fall in the tuberculous death rate than in any great city.

We inoculated subcutaneously three full-grown male guinea pigs with thirty-five, seventy-five and one hundred and twenty-five virulent human tubercle bacilli respectively. The inoculations were made in the nipple area and it was possible to follow the course and degree of infection in the inguinal glands. The largest number produced the most rapid infection and in this pig tubercle bacilli were obtained by puncture of the neighboring inguinal glands after three weeks, and the animal was then killed and showed extensive visceral lesions. Tubercle bacilli could not be obtained from the guinea pig receiving thirty-five until the animal was killed six weeks later, and then the disease was strictly limited to the inguinal glands. The lesions in the guinea pig receiving seventy-five bacilli were intermediate in degree to the other two pigs.

The probability is that in infection from dust by inhalation we do not receive very large numbers—at least not millions—of bacilli, probably only a few hundred or less. Infection by the intestinal route requires a much larger number in all experiments than infection by inhalation. Tuberculosis is peculiarly a disease in which both the virulence of the bacteria as well as the numbers received determine the course of infection, and the latter factor may to a certain degree possibly outweigh the former.

Probably a third and important factor is the frequency of dosage. It is recognised that constant contact with the careless consumptive is the cause of some of the most serious infections, and the experience of Lieb with the subcutaneous inoculations of virulent bovine bacilli in rabbits later referred to, would seem to be a laboratory imitation of this condition.

It occurred to me nearly six years ago, after watching the ingenious technic of Professor M. A. Barber,[4] by which he was able to isolate single bacteria, that could we apply this mechanical principle and inoculate animals with increasing numbers of virulent bacteria, beginning with one, we might be able to produce successful immunity. We[5] first worked with mice and anthrax bacilli. It was known that one twenty-millionth of a drop of anthrax broth culture would kill a mouse in twenty-four hours. By inoculating first one bacillus and gradually increasing the numbers we were safely able to give mice doses which inoculated all at one time meant certain death.

Barber[6] followed this work out further, but found that with such a virulent organism as the anthrax bacillus and such a susceptible animal as the mouse much immunity could not be procured.

We[7] next inoculated in a similar manner guinea pigs with virulent human tubercle bacilli. We found that about twenty-five virulent human tubercle bacilli injected subcutaneously in one dose, would often prove fatal to an adult guinea pig.

In one animal we continued the inoculations at weekly intervals for nine months and in all injected safely about one hundred and fifty thousand virulent human tubercle bacilli. This pig was killed and no tuberculosis was found. Portions of its organs and lymph glands were injected into another pig and failed to produce tuberculosis.

Lieb,[8] working in our laboratory, carried on similar work on rabbits with the bovine tubercle bacillus. He was able, by this method, to begin inoculating a litter of rabbits at the moment of birth and to continue the inoculation with safety as they grew.

His work showed that by inoculating increasing numbers of living virulent bovine bacilli there was evidence of immunity production in both young and adult rabbits. Such immunity apparently depended both upon the age of the rabbit and the size of the increasing doses.

For instance Lieb found that in rabbits two weeks old he could safely inoculate at weekly intervals beginning with one bacillus and increasing by the ratio 2, 4, 6, 8, 10, 12; yet should the sequence be 1, 5, 10, 15, 20, etc., tuberculosis was produced. When, however, the rabbits were ten weeks old they could submit to the latter series of inoculations without infection. It was of special interest that in one of his experiments a rabbit receiving a dosage of 1, 25, 50, 100, 200, etc., bacilli died sooner than another of the same litter receiving 1/10 cc. of a thick emulsion of the same culture, evidently the result of an acquired hypersusceptibility.

In the spring of 1910 we[9] carried the work a step farther by inoculating some twelve monkeys (*Macacus rhesus*) with virulent human tubercle bacilli.

The animals were thoroughly tested with tuberculin and shown to be uninfected before the experiments began. Thirty-five bacilli of the culture of human bacilli employed, produced tuberculosis following subcutaneous injection into a guinea pig.

The inoculations * were kept up at weekly intervals over a year, and up to date, after two years, the animals are perfectly healthy. Two of the monkeys received enough virulent tubercle bacilli to kill over ten thousand guinea pigs, and yet these monkeys weighed only as much as three full-grown guinea pigs. The monkeys have been repeatedly tested with tuberculin during the course and none have reacted except as mentioned below.

Six monkeys have been killed and a thorough search has revealed no trace of tuberculous disease. To make no mistake, due to overlooking possible foci of disease, pieces of the different organs and lymphoid glands of three of the animals were injected into guinea pigs and no infection of these was produced.

We have not yet learned the lowest possible number of virulent human tubercle bacilli which will infect a young monkey.

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* The following plan indicates how each animal was treated:

1. Control.
2. 25 bacilli in one dose and no further inoculations.
3. 100 bacilli in one dose and no further inoculations.
4. 200 bacilli in one dose and no further inoculations.
5. Increase slowly, 1, 3, 5, 10, 15, 20 bacilli, etc.
6. Increase slowly.
7. Increase rapidly, 1, 5, 10, 20, 50, 100 bacilli, etc.
8. Increase rapidly.
9. Increase slowly, 5, 10, 15, 20, 25, 30 bacilli, etc.
10. Increase rapidly, 5, 15, 45, 75, 125, 200 bacilli, etc.
11. Control.
12. 50 bacilli at one dose and no further inoculations.

We were surprised, however, to find the resistance of monkeys to the culture we employed very much greater than that of guinea pigs. Two hundred and fifty as a single initial dose failed to give one monkey tuberculosis, whereas thirty-five infected a guinea pig.

In testing the monkeys for possible tuberculous infection the conjunctival and intradermal methods were employed.

For the intradermal test one twentieth of a milligram old tuberculin was injected and the skin fold measured according to Römer's directions. In the third test of this kind, by mistake 20 milligrams were injected, with the result that monkeys Nos. 8, 10, and 11 gave reactions.

Monkey No. 11, a control, was immediately killed, but no trace of tuberculosis could be found. The products resulting from maceration of various lymph glands, portions of lungs, liver, spleen and kidneys, were injected into a guinea pig, but no tuberculosis resulted.

We felt, therefore, that the positive skin reaction resulted from tuberculo-protein sensitization.

As a final test we followed the work of White and Fox [10] of Philadelphia and, having kept temperature records for several successive days at 3 p. m., injected 5 milligrams old tuberculin.

The temperature was to be taken every three hours over a period of two days, but in no monkey was there a rise. Monkey No. 1., a control, alone gave the typical night drop subsequent to the injection. The temperature of monkey No. 2, at the end of the 48 hours, kept significantly low. The monkey appeared very sick and we thought he would die. He recovered the next day, but we thought it best to kill him. A thorough search using every means to reveal tubercle bacilli, and also the injection of macerated extract of various organs into a guinea pig, failed to give evidence of any tuberculosis having existed. We therefore concluded that this phenomenon must have depended upon tuberculo-protein sensitization.

In general there seems to have been a suggestion of interference in the normal night temperature drop. This may be due to tuberculo-protein sensitization or possibly to the presence of antibodies resulting from the inoculation of the living bacilli. I am inclined to the latter view, because monkey No. 1, which had received successive tuberculin injections in the tests, just as the others had done, showed no change in the night drop of temperature.

From time to time we have made differential blood counts. In all the lymphocyte percentage has kept high, and this fact has been of some value to show that no infection has taken place.

To attempt the same experiments on children would be cause for grave anxiety. We have shown that such inoculations were harmless and even of some benefit to tuberculous individuals, but this was entirely a different matter from inoculating the non-infected.

A most unusual opportunity, however, was offered by a distinguished scientist dying of tuberculosis, who requested me to inoculate his two children, aged nine months and three years, in a similar manner to that by which we had succeeded with the monkeys—experiments which this gentleman watched with great interest. The children were inoculated with bacilli from a culture of which 150 infected a guinea pig as indicated by the following figures:

NUMBER OF BACILLI INJECTED.

Date	No. bacilli	Date	No. bacilli	Date	No. bacilli
10/20/10	1	11/25/10	18	12/29/10	100
10/27/10	3	12/ 1/10	25	1/ 5/11	125
11/ 3/10	5	12/ 8/10	35	1/12/11	150
11/10/10	8	12/15/10	50		
11/17/10	12	12/22/10	75		

Total number bacilli received by each child, 607.

The following children have been inoculated as the table indicates. The culture used, however, weakened in virulence and we have not ascertained yet the exact number to cause infection in a guinea pig.

The mother of these children, it may be mentioned, was also found to be actively tuberculous. The children were first tested by means of the von Pirquet skin tuberculin test and reactions were found to be negative. The inoculations were started with one bacillus and increased at weekly intervals until six hundred had been injected. The von Pirquet tests were again applied and found negative and some months after the inoculations of the live germs had ceased were once more found negative.

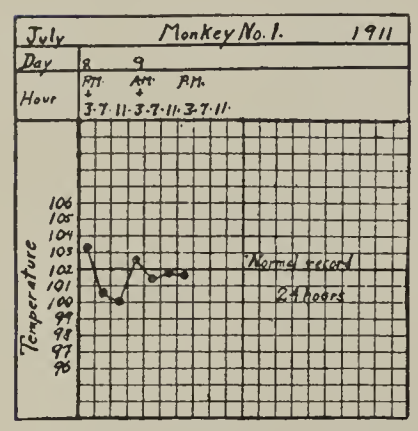
All were tested by skin tuberculin reaction 3/16/12, and all were negative.

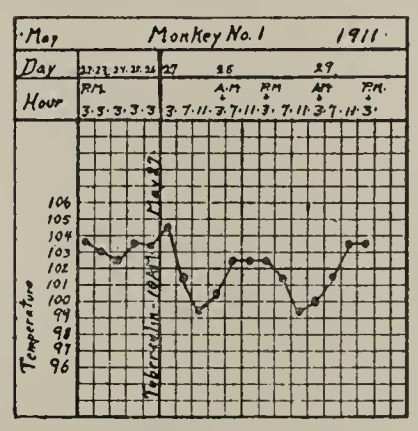
Children.	Age.	Date.																						
		8/29.	8/31.	9/9.	9/18.	9/24.	9/30.	10/7.	10/14.	12/7.	12/14.	12/22.	12/28.	1/4.	1/11.	1/18.	1/22.	1/29.	2/5.	2/12.	2/19.	2/25.	3/4.	3/11.
L.	4 mos.	..	..	..	..	..	..	..	..	1	5	10	15	20	25	35	50	75	100	125	150	200	250	300
V.	6 yrs.	2	4	6	10	15	20	30	40	..	..	..	..	..	..	..	15	25	35	45	65	100	125	150
G.	4½ yrs.	1	2	5	8	12	15	26	35	..	..	..	..	..	..	..	15	25	35	45	65	100	125	150
R.	3 yrs.	1	1	4	8	12	15	24	30	..	..	..	..	..	..	..	15	25	35	45	65	100	125	150
EL.	2 mos.	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	5	8	12	25	35	45	55

It may be conjectured that in view of a certain degree of racial immunity in man greater than in the monkey, probably a larger number of tubercle bacilli may be needed to infect a child than a monkey. We have, however, not considered this possibility but have inoculated the children with more cautiously graded numbers than we did the monkeys and with a less virulent culture. We may in time learn that perhaps a single dose of a few hundred bacilli inoculated subcutaneously will protect our children, but for the present it is most important to be unusually cautious, and regard the possibility that children can be infected as easily even as guinea pigs.

The question as to whether the subcutaneous inoculations will provoke an immunity which will protect the lungs we will work out further in the monkeys. It has been shown, however, that an infected guinea pig will resist a second infection of moderate degree just as well by the lungs as by the subcutaneous tissues. It would seem very necessary to begin such vaccination at birth, whilst the infant is being nursed by the mother.

It is possible in hydrophobia to succeed in producing immunization after infection, on account of the long incubation period of this disease. This can hardly be possible in children in


July
Monkey No. 1.
1911
Day
Hour
Temperature
Normal record
24 hours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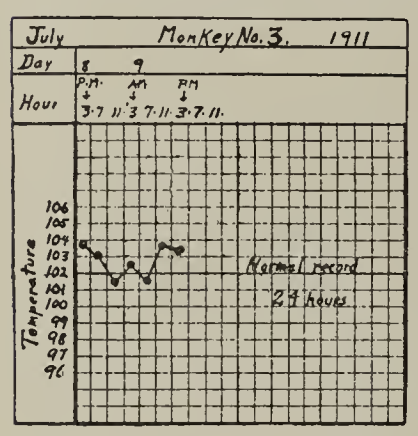
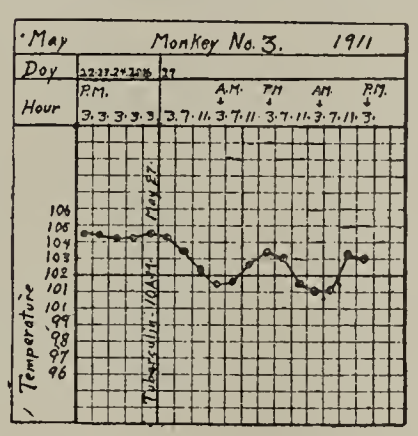
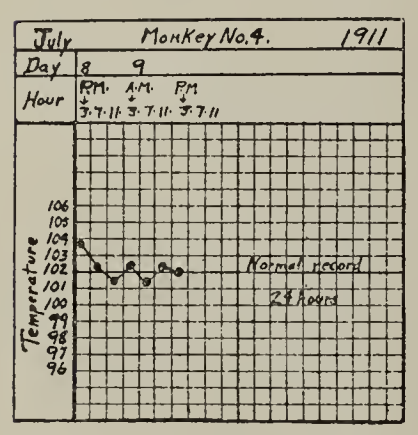
Monkey No. 1
1911
Day
Hour
Temperature
Tuberculin-10 A.M. May 27


July
Monkey No. 3.
1911
Day
Hour
Temperature
Normal record
24 hours


May
Monkey No. 3.
1911
Day
Hour
Temperature
Tuberculin-10 A.M. May 27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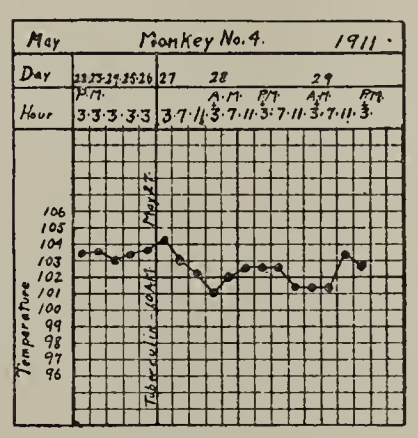
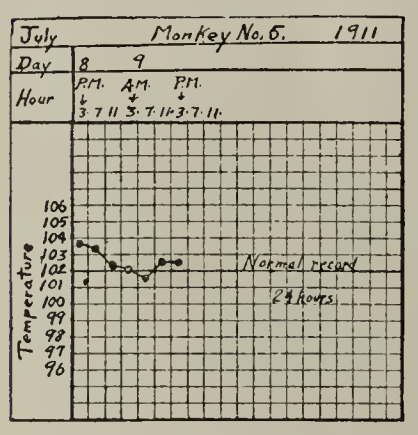
Monkey No. 4.
1911
Day
Hour
Temperature
Normal record
24 hours


May
Monkey No. 4.
1911
Day
Hour
Temperature
Tuberculin-10 A.M. May 27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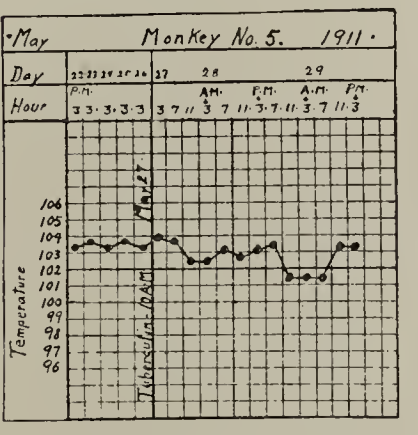
Monkey No. 5.
1911
Day
Hour
Temperature
Normal record
24 hours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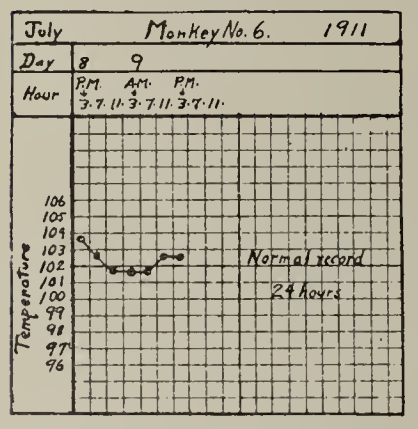
Day
Hour
Temperature
Tuberculin-10 A.M. May 27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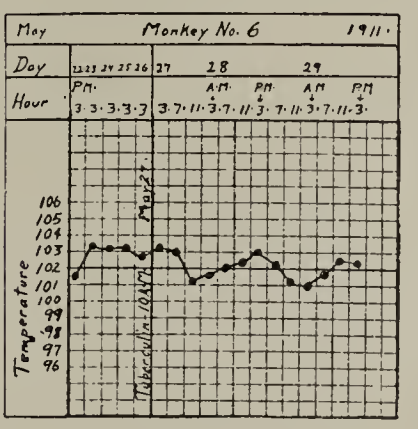
Monkey No. 6.
1911
Day
Hour
Temperature
Normal record
24 hours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Monkey No. 6
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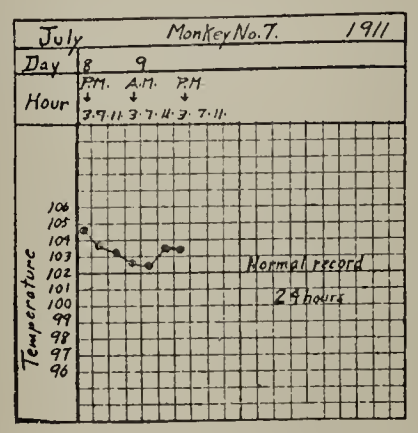
Day
Hour
Temperature
Tuberculin-10 A.M. May 27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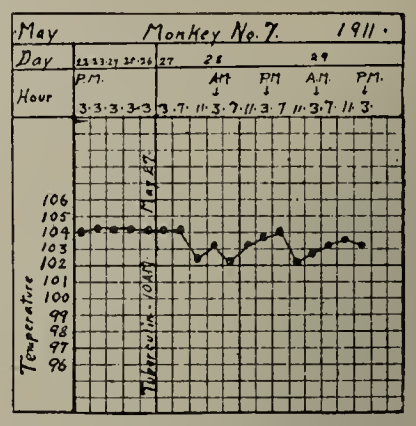
Monkey No. 7.
1911
Day
Hour
Temperature
Normal record
24 hours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1911
Day
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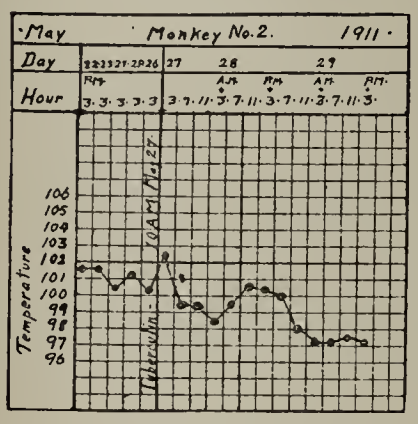
Temperature
Tuberculin-10 A.M. May 27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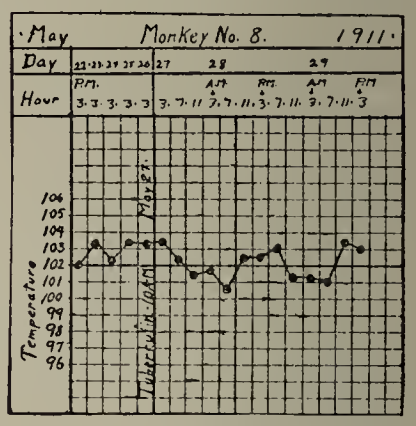
Temperature
Tuberculin-10 A.M. May 27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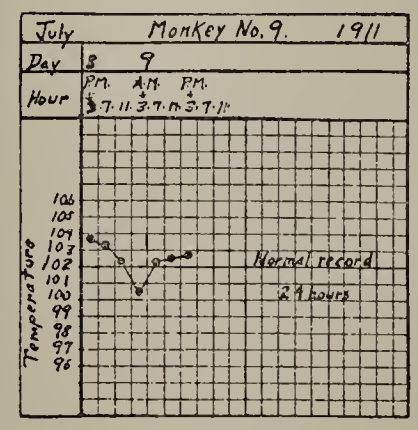
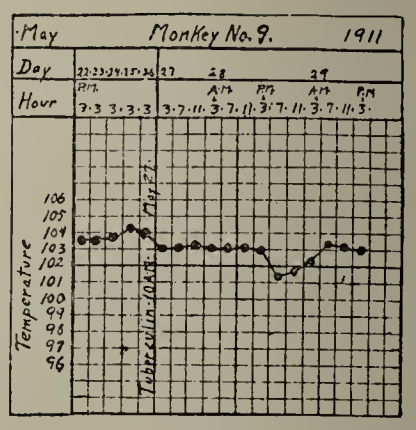
Temperature
Tuberculin-10 A.M. May 27


July
Monkey No. 9.
1911
Day
Hour
Temperature
Normal record
24 hours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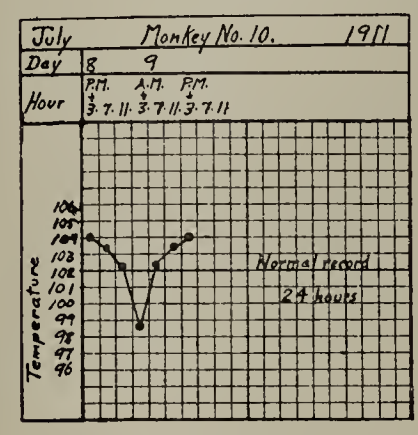
Tuberculin-10 A.M. May 27


July
Monkey No. 10.
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Day
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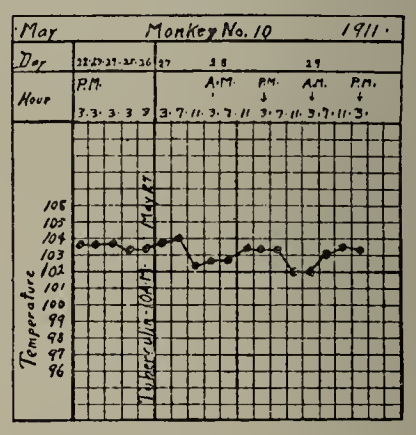
Temperature
Normal record
24 hours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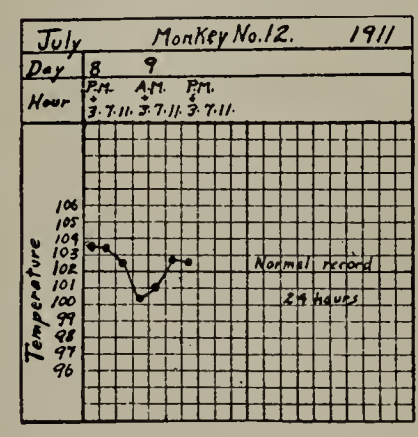
Temperature
Tuberculin-10 A.M. May 27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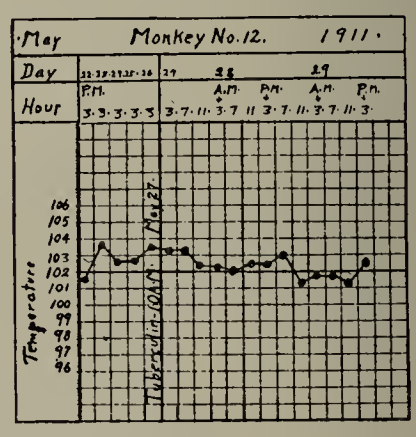
Monkey No. 12.
1911
Day
Hour
Temperature
Normal record
24 hours


May
Monkey No. 12.
1911
Day
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Temperature
Tuberculin-10 A.M. May 27

tuberculosis for we have found one thousand virulent bovine bacilli infect calves in less than a month so that it would seem better to err in beginning too early, and in children born to tuberculous parents to remove them at birth whilst the vaccination proceeds.

Metchnikoff, in his book "Immunity and Infective Diseases," quotes Massart as saying, "vaccination effects an education of the leucocytes; these latter become so adapted that they can approach the virulent micro-organisms." He goes on to say later that "The acquisition of immunity against micro-organisms is, therefore, due not only to the change from negative to positive chemotaxis, but also to the perfecting of the phagocytic and digestive powers of the leucocytes." He quotes the work of Delezenne in which he proved the phagocytes of a dog could be educated to digest more and more gelatine, when at first they digested it but feebly. This indicates an acquired digestive power. Such acquired digestive power would seem to be most necessary in the defence against tuberculosis.

All our inoculations have been made subcutaneously and the work related would appear to refute Koch's positive statement that "We shall not succeed in habituating the organism to absorbing entire bacilli which have been injected subcutaneously; and by injecting small quantities of them we shall not habituate the organism to absorbing more."

We found for instance in the series of inoculations referred to that when we reached 3000 to 5000 bacilli almost invariably a lump occurred at the inoculation site which would take from one to three weeks to disappear.

This occurrence coincides with the statement of Metchnikoff that "In vaccinated animals the local reaction (in such diseases as anthrax, streptococcus infections, etc.) is more marked, and the exudation very rich in leucocytes. The destruction of the micro-organism, inside these cells, takes a longer or shorter time according to circumstances; but in the end it is always complete."

Following these experiments we tested the monkeys for the presence of antibodies. Emery's [11] method of measuring quantitatively the specific antibodies in a given serum was made use of, but failed to demonstrate their presence. Antibodies were also tested for by means of the meiostagmin reaction described by Ascoli [12] and Izar.[13] None were demonstrated. The phagocytic index which was devised by Neufeld [14] and Hune and Klein and advocated by Meakins [15] seemed to indicate an increased phagocytic immunity in monkey No. 7.

It would seem necessary to recognise two forms of immunity in tuberculosis, the apparent immunity of the infected to reinfection indicated by the phenomenon of Koch, and what may be termed true immunity. In the latter no tuberculin reaction could be expected and it would appear to be the ideal form of immunity to be sought.

It is this form of immunity therefore that we have hoped to attain by this method of inoculation and we believe that this has been achieved.

We have had some forty volunteers for treatment with inoculations of living tubercle bacilli. The procedure has been similar to that reported for the production of immunity. We have not inoculated beyond 5000 bacteria. In general the patients have been in the Turban III class. The results will be given in detail at another time, but it can be stated now that some good would seem to have been accomplished and never has harm resulted. We feel that perhaps better results would appear from larger doses. The future might indicate the necessity for enough bacilli to be inoculated subcutaneously to produce a local lesion. It is well known that a local lesion in some part of the body is frequently of much benefit to tuberculous lung processes.

White Blood Cells.

The defense of the organism against the tubercle bacillus has in general been ascribed to the tissue cells rather than to the white corpuscle. From our own work in studying the white corpuscles of patients with pulmonary tuberculosis we feel we can thoroughly agree with the reported work of Craig [16] of Philadelphia, who finds that the earlier the stage of pulmonary tuberculosis the fewer are the leucocytes, but the earlier the stage the more numerous are the lymphocytes and mononuclears, and the fewer are the polymorphonuclears.

We have shown that the differential blood picture is of some value in indicating the presence of tuberculosis and also its prognosis, as the following chart will testify:

Polymorphonuclears	Mononuclears			Eosinophiles	Mast-cells
	Average	Mean	Extremes		
CURED CASES OF PULMONARY TUBERCULOSIS. 57 cases; 100 counts.					
55.5	41.7	41	25-63	2.3	0.5
IMPROVING CASES. 43 cases; 114 counts.					
5.49	38.5	37	18-54	1.7	0.4
STATIONARY CASES. 44 cases; 125 counts.					
63.6	34.4	33	18-50	1.6	0.4
CASES PROGRESSING UNFAVORABLY. 43 cases; 159 counts.					
70.8	27.5	27	14-46	1.3	0.4

In following the later work on immunity investigations in tuberculosis, one is struck with the growing importance placed upon the lymphocytic element as the chief machinery of the organism's defense. Bartel [17] states that the behavior of tubercle bacilli that have entered the body through natural channels indicates a protective action on the part of the cells of organs, and especially of lymphocytes, against infection.

Recent researches by Opie [18] show that the epithelioid cells in tuberculous tissue contain an enzyme exactly similar to that possessed by the large mononuclear leucocytes of the circulating blood. His work indicates that these epithelioid cells may in reality be emigrated large mononuclear leucocytes, which they very closely resemble.

Nichols [19] has shown in the histological study of the lesions of immunized rabbits that the reaction to infection on the part of the lung of the vaccinated animals is much more rapid and intense than in the control or non-vaccinated animals. He intimates that the tissue cells could hardly multiply quickly enough to account for the excess of epithelioid cells, and that more probably most of these are leucocytes from the blood.

The participation of the lymphoid cells in tubercle formation has long been known, and Metchnikoff has claimed the giant-cells to be accumulated macrophages. In experimental tuberculosis the response of tissue to a beginning infection is accompanied by an accumulation of polymorphonuclear leucocytes, but these are soon deplaced by epithelioid and lymphoid cells.

Claude and Zaky [20] in 1902 showed in animals which best resisted tuberculous infection the presence of many large mononuclears. Halbron [21] in 1903 also emphasized the importance of these cells. In 1905 Ullom and Craig, in summarizing their investigations on blood studies in pulmonary tuberculosis, stated that they had received the impression that the actual increase in the lymphocytes corresponded to increased resistance of the patient to tuberculosis. It is also an interesting fact that the age period of greatest outbreak of pulmonary tuberculosis, is not that of childhood, when the percentage of lymphocytes is greatest.

In addition to the evidence given as to the defensive behavior of lymphocytes, Daels [22] has shown that the von Pirquet skin reaction to tuberculin is characterized by the collection of lymphoid cells at the irritated area. Josué [23] shows that in localized experimental tuberculosis in rabbits the bone-marrow responds to infection by a very intense proliferation of the mononuclear leucocytes, and also that the subcutaneous injection of tuberculin will bring about similar marrow activity.

Cadbury [24] found in patients dying of pulmonary tuberculosis that if the bone-marrow was found proliferated, it was practically the rule to find a considerable number of lymphocytes.

It is especially noteworthy that two years ago Bergel [25] in Germany, and Marie and Fiessinger [26] in France, made the important discovery that the lymphocytes contain a ferment of lipolytic power capable of splitting wax and fax into glycerin and fatty acids. Following Opie's method of nomenclature, we suggested for this ferment the name of lympholipase. It has long been known that at least 30 per cent by weight of the body of the tubercle bacillus is composed of waxy substances, and the chronicity of tuberculosis has been thought to be due to the difficulty the defensive mechanism of the host must have to destroy this waxy substance. It is possible too that the polymorphonuclear cell contains some lipase. We were able to corroborate Bergel's observation by finding that pus from a cold abscess digested the surface of beeswax on which it was placed.

Pribram [27] believes in a lipolytic ferment being present in the blood, but does not feel sure, on account of his failure in a small number of experiments, that it is yet completely proved that lipase originates in the lymphocytes.

We have ourselves studied the lysis of tubercle bacilli by the lymphocytes of cockroaches and grasshoppers. These insects would seem to have entirely this type of cell, corresponding to our large lymphocytes. Injections of tubercle bacilli can readily be made into one hind leg, and at various intervals lymphocytes containing tubercle bacilli in all stages of digestion can be found by withdrawing some circulating fluid from the other hind leg.

We have been struck by the length of time necessary for this digestion, often several days and not several hours only, as might be thought.

Fiessinger [28] has published a paper on the part played by lipase in the defense against tuberculosis. Plates accompanying his paper illustrate the lysis of tubercle bacilli by the lymphocytes of the bee-moth larva.

Fiessinger concludes that the lymphocytes furnish lipase, which destroys the waxy parts of the tubercle bacillus, and that it is then necessary for the polymorphonuclear leucocytes to appear with their leucoprotease, which only works in an alkaline medium, to complete the digestion. He would seem to overlook the fact that the lympholipase, by splitting wax into fatty acid and glycerin, might supply the acid medium in which the lymphoprotease could act.

Then, too, we know that complete lysis can proceed in insects which have no polymorphonuclear leucocytes, but only lymphocytes.

It has been shown by Opie [29] that the injection of living leucocytes, consisting of an approximately equal suspension of polymorphonuclear and of mononuclear cells obtained from normal dogs and injected into dogs which have been artificially infected with the tubercle bacillus, can inhibit the development of tuberculous lesions. This would seem to show the value of increasing the numbers of leucocytes.

Manwaring [30] has recently shown that subdural inoculations of tubercle bacilli in dogs produce meningitis. A suspension of leucocytes procured from another dog injected subdurally delays the progress of the disease and prolongs life.

During an epidemic of whooping-cough in the fall of 1908 we attempted to diagnose this disease from an epidemic of catarrhal bronchitis by means of differential leucocyte counts. Barach [31] in July 1908 had recalled attention to the increased percentage of lymphocytes which characterized pertussis, and showed the value of differential counts in establishing a diagnosis. He found both a leucocytosis and a lymphocytosis. The smaller lymphocytes first increased, and the large lymphocytes followed the course of the small ones, reaching their greatest numbers, however, after the small lymphocytes had reached theirs.

After investigating several patients who presented high lymphocyte counts, and yet who clinically we felt certain had only a *micrococcus catarrhalis* infection, we were led to examine the blood of normal children of ages from six to twelve, and found the percentage of lymphocytes higher in all than the normal for sea level.

It happened that at the same time some experimental work

was undertaken on rabbits to ascertain what blood changes, if any, could be brought about by inoculations of mercury, and in the light of the growing importance placed upon lymphocytes in the problem of immunity to tuberculosis, especial attention was paid to see if these elements could be increased.

The result of differential counts on normal rabbits showed that they, too, had a higher percentage of non-granular mononuclear cells than sea-level rabbits, as the following figures indicate:

	Polymorphonuclears	Mononuclears	Eosinophiles	Mast-cells
CHILDREN.				
Colorado Springs.	37.3	60.3	2.0	0.4
Sea Level.....	53	46	1.0	0.0
ADULTS.				
Colorado Springs.	54	43.6	2.0	0.4
Sea Level	61.7	37.4	0.9	0.0
RABBITS.				
Colorado Springs.	31	65	0	4
Sea Level.....	43	52	0	5
GUINEA PIGS.				
Colorado Springs.	19	81	0	0
Sea Level.....	60	40	0	0
MONKEYS (*Macacus Rhesus*).				
Colorado Springs.	31	65.9	1	0
Sea Level *.....	40	55	4	1

* From Hektoen's "Experimental Measles in Monkeys."

The above chart is compiled from a large number of counts. The specimens were taken usually about noon.

It is notorious that observations on white blood cells in regard to both numbers and characters are open to wide variations.

It is recognised that many factors such as sleep, digestion, exercise or time of day render exact comparisons between white cell counts very treacherous, and in addition the techniques for both total white cell counts and differential percentage estimations are also open to not inconsiderable error.

The explanation of the different normals given by various authorities probably lies in these difficulties for exact determinations and comparisons.

Levaditi [32] gives the normal white blood cells per cmm. in healthy adults as 7000-8000, whereas Kjer-Petersen [33] claims 4000-5000 as correct.

The differential white cell picture is according to

	Polymorphonuclears.	Lymphocytes and large mononuclears.	Transitionals.	Eosinophiles.	Mast cells.
Jolly [34]	61.7	35.2	2.2	0.9	
Ehrlich [35]	71	23.5	2	3	0.5

Bunting, of Madison, Wisconsin, has recently published a paper calling attention to the percentage of the different kinds of leucocytes quoted in the literature and making comparisons with his findings at Madison. He suggests that the difference may be due to the fact that in the employment of Ehrlich's original stain some of the lymphocytes did not show up, as they do with the modern Wright stain. Bunting's work, however, was carried out at an altitude of about one thousand feet and his twenty-five reported cases averaging 42% lymphocytes were healthy young adults, mostly students. The following chart is prepared from differential blood counts made from students at Colorado Springs and Harvard.

STUDENTS, HARVARD.
18 cases; 18 counts.

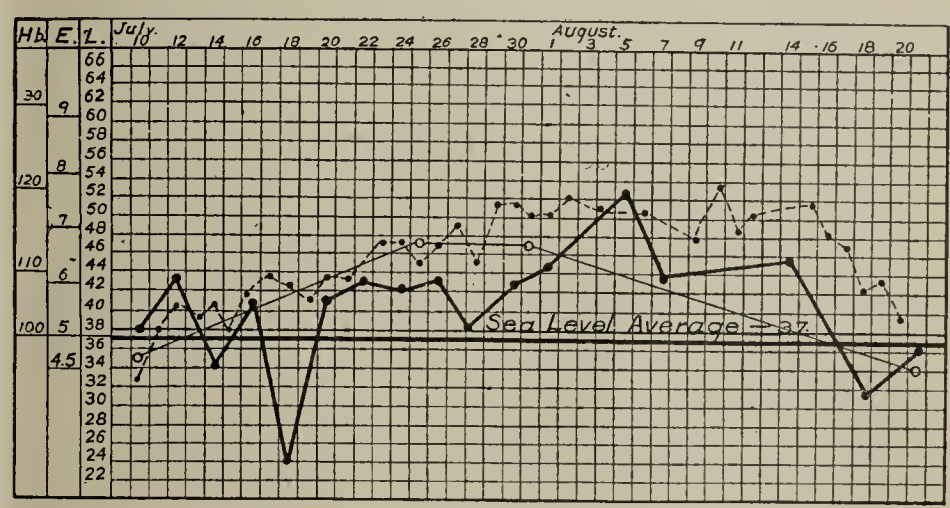
Polymorphonuclears	Mononuclears			Eosinophiles	Mast-cells
	Average	Mean	Extremes		
59.5	38	37	27-56	2	0.5

STUDENTS, COLORADO COLLEGE.
18 cases; 18 counts.

48.5	49.5	52	37-66	1.7	0.3

The following charts are prepared from blood examinations made on Haldane and Douglas of Oxford, Henderson of Yale and Schneider of Colorado College during the recent expedi-

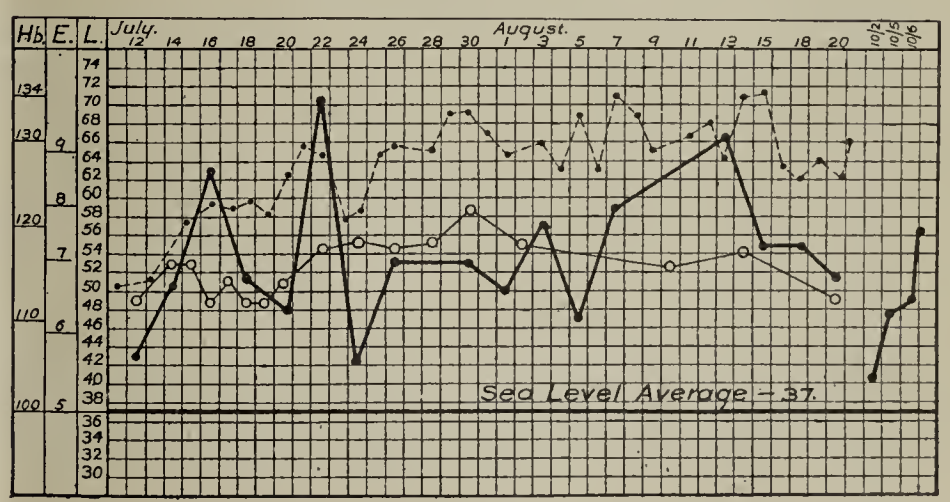
Pike's Peak, 14,000 Ft. J. S. H. 1911.
Expedition on Peak lasted from July 12 to August 16.



------- Hæmoglobin, Hb.
——— Red Cells, E.
——— Lymphocytes, L.

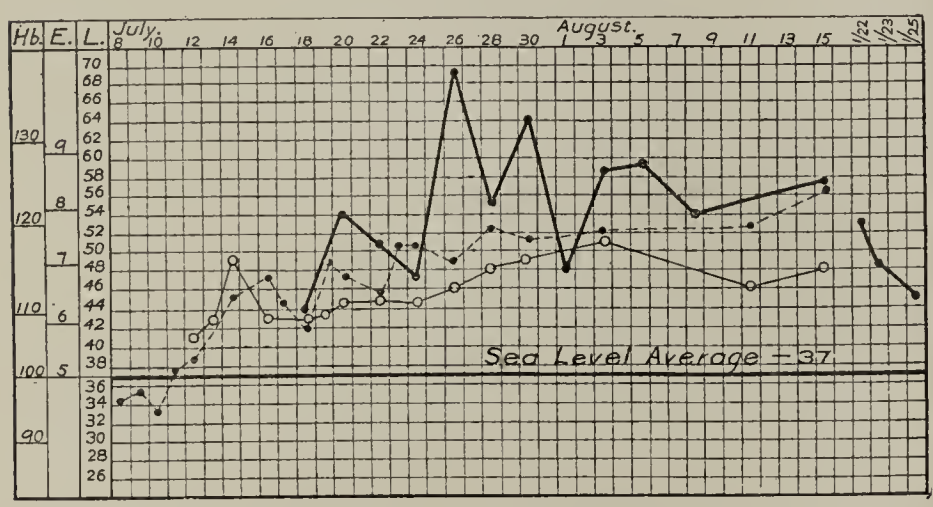
J. S. H. was suffering from a chronic infection and had constantly 15,000 white blood corpuscles.

Pike's Peak. Y. H. 1911.

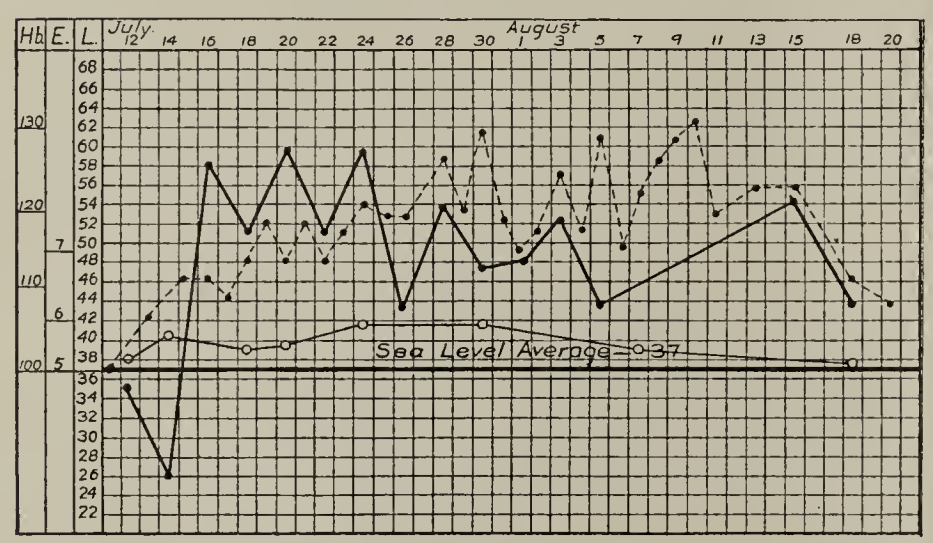


tion to be summit of Pike's Peak, Colorado, for the study of mountain sickness.*

PIKE'S PEAK. E. C. S. 1911.



PIKE'S PEAK. C. G. D. 1911.



In Charts 2 and 3 the red blood corpuscles indicate an early initial rise and then decline; later, an overproduction. Charts 2, 3 and 4 indicate the overproduction, later referred to, of lymphocytes after 2 weeks.

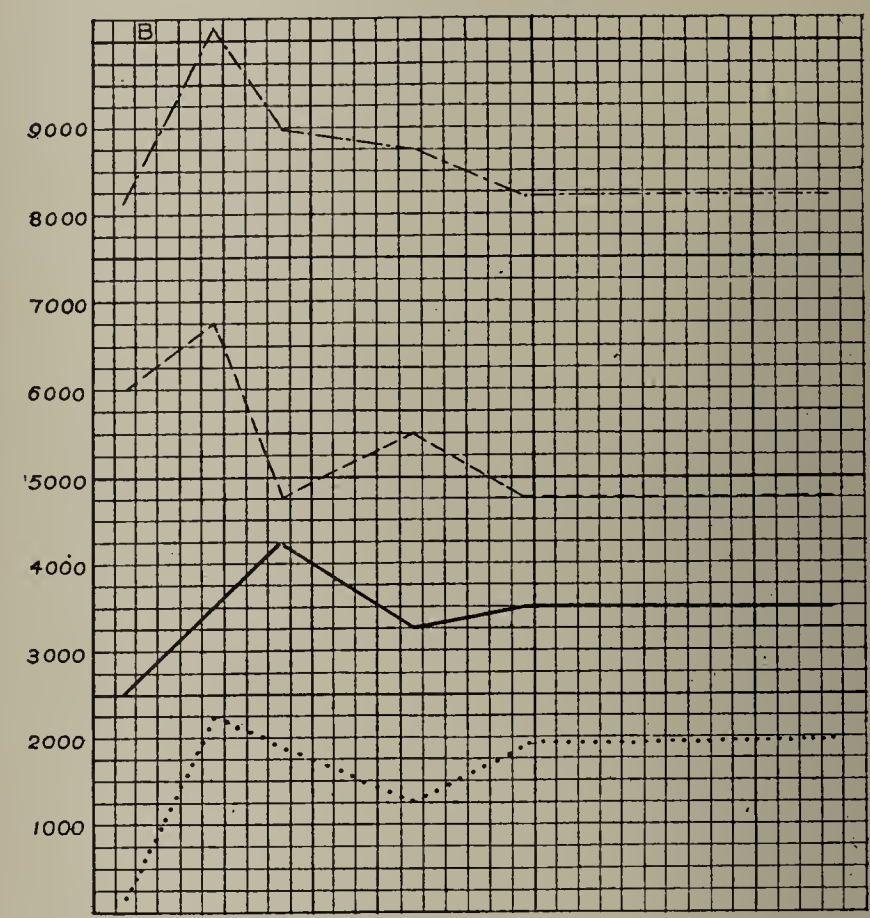
Zuntz[36] explains the increased numbers of erythrocytes in high altitudes as due to hyperplasia of the bone-marrow, and by his experiments on dogs, it would seem, conclusively demonstrates this.

By colored plates he pictures the changes of blood smears due to this increased marrow activity, and in a specimen of blood taken from the marrow vein of a dog previously almost bled to death, he shows, besides the appearance of nucleated red cells, the presence of large lymphocytes.

Following our observations on the effect of altitude in increasing the lymphocytes it was now argued that if bone-barrow hyperplasia provoked the increase of mononuclears reported, then artificial hyperemia of accessible bones might yield the same result. To this end a rubber bandage was applied as a tourniquet to the legs, as high up the thighs as

* The expedition discovered that at altitudes such as Colorado Springs and Pike's Peak, the lung cells themselves develop and secrete oxygen from the air and throw it into the blood. It was also conclusively shown that mountain sickness is due to lack of oxygen. The hæmoglobin and the red corpuscle counts were made by the members of the expedition, and are published by their courtesy.

CHART TO SHOW EFFECT OF ALTITUDE (6000 FEET) ON HEALTHY MAN COMING FROM SEA LEVEL.



On arrival. 1 week. 2 weeks. 3 weeks. 3 months. 1 year.

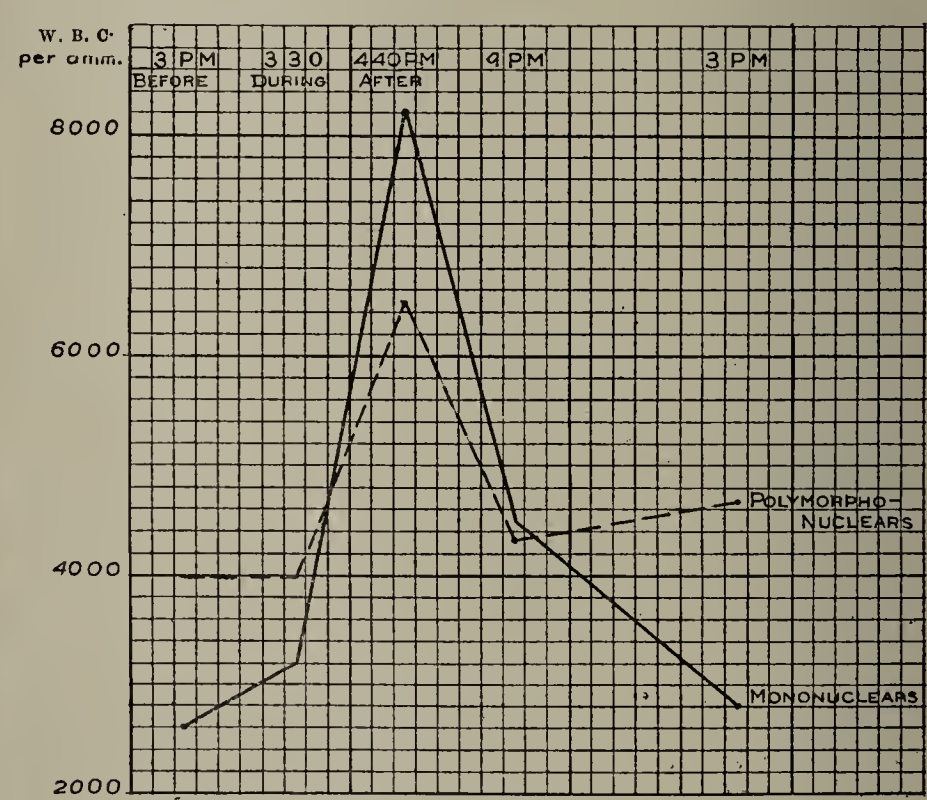
Explanation of Chart —.—.—. Total leucocytes per cmm. ------ Total polymorphonuclears per cmm. ———— Total mononuclears per cmm. ..... Large lymphocytes per cmm.

Notice overproduction of mononuclears after 2 weeks then drop. This would appear to be a similar biological phenomenon to Weigert's theory applied to the overproduction of amboceptors.

Notice the same in regard to both red blood cells and lymphocytes in several of the Pike's Peak charts.

possible, with sufficient pressure to interfere with the return venous flow, but not enough to obstruct the arterial.

The following chart represents the results of the first application of this method to man:

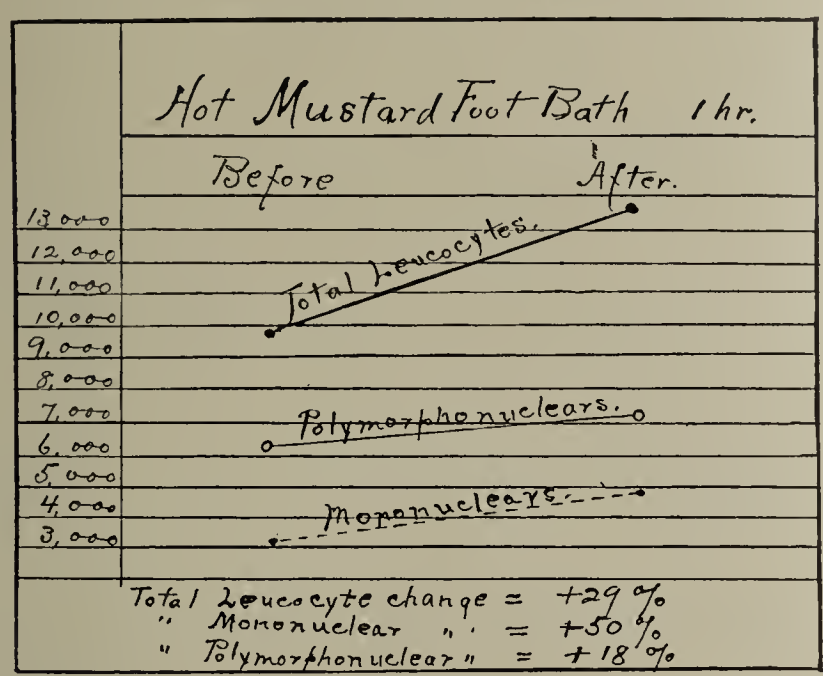


Mononuclear increase = 215%.
Polymorphonuclear increase=60%.

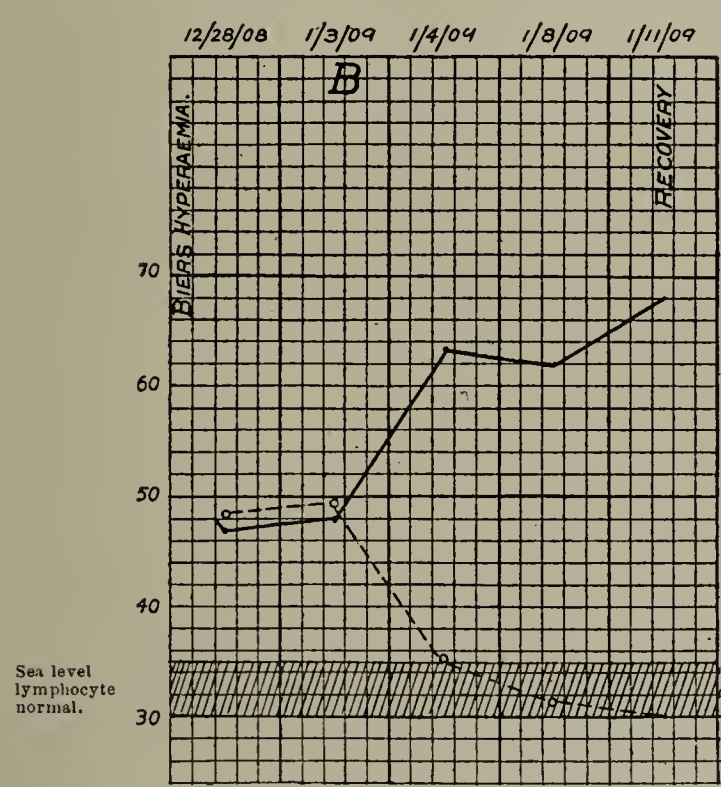
We found also that lymphocytosis could be produced by constant hyperemia of accessible long bones, as the following observations attest. The patients applied to their upper arms, day and night, a garter elastic, one inch wide, which was just tight enough to leave an indentation in the skin after removal. They suffered no discomfort, neither did the arms visibly swell. The following is an example:

Miss V. Turban III.—White blood corpuscles, 13,000. Lymphocytes, 29%. Two weeks hyperemia of both arms with garters: White blood corpuscles, 25,000. Lymphocytes 69%.

It was next questioned what the results of a hot mustard foot-bath might be on the blood picture; theoretically, it was expected a similar change would take place. The following is the result of such an experiment on a healthy male adult.



Several cases of tuberculous disease in the leg treated by Bier's hyperæmia yielded similar lymphocyte increase, as is seen in the chart below.



Small tuberculous abscess of tibia following blow received in hockey game.

——— Lymphocytes.
------ Polymorphonuclears.

We found with the continued arm hyperemia that about two weeks were required to produce the greatest results. After this time the patient's sputum will decrease, especially the thick yellow portion. In one patient who estimated that she expectorated her body weight in eight months the amount was reduced to one-quarter ounce daily. In some patients after several weeks treatment both temperature and pulse dropped.

The marrow as an organ is capable of enormous increase in work. The yellow marrow can be replaced by blood-forming marrow and even the bony lamellæ can be removed to make room for red marrow. We have used daily hot mustard foot-baths in order to provoke more activity in the bone marrow of the legs. Inasmuch as the fight against the tubercle bacillus is so largely one of blood cells the more marrow we can urge to work the better.

In some researches we conducted on rabbits we found that the red cells are also increased by marrow hyperemia, as the following tables show:

Normals—6 counts on 6 rabbits.....Average, 6,300,000
Normals—4 rabbits after one-half hour hyperemia .....Average, 8,100,000

Controls, R. 1, 2, 4, 5, and 6.....Average, 6,150,000
Hyperemias, R. 7, 8, 10, 11, and 12.....Average, 9,400,000

Being able to produce so large a lymphocytosis it was natural to question what would happen to the cell picture in the sputum. It was found that the lymphocytes appeared in the sputum in very large numbers, almost entirely replacing the polymorphonuclear cell.

Lymphocyte pus cells on careful searching could be found containing fragmented tubercle bacilli. With some patients the numbers of tubercle bacilli in the sputum appeared to diminish. That such cells appeared in the sputum indicated migration from the blood stream. The blood of such patients was therefore taken for opsonic tests. By means of these it was shown that the large lymphocyte and especially the large mononuclear and transitional cells had decided phagocytic powers. Making repeated observations at different intervals it was found that after forty-eight hours incubation some digestion and fragmentation of tubercle bacilli could be observed within these cells. The polymorphonuclear leucocytes did not seem to have this power.

The cover slip preparation of blood taken from individuals submitting to continued arm hyperæmia gave evidence of a large increase in blood platelets. We are at present attempting to ascertain the exact increase in these elements and also to determine whether they are increased by the effect of altitude, which we think possible.

The types of nongranular mononuclear cells increased by marrow hyperæmia are especially the large lymphocyte, the large mononuclear and transitionals. Occasionally also plasma cells are seen.

The effect of altitude and of bone marrow hyperæmia on the blood are therefore very similar to that of chronic carbon monoxide poisoning. In this, besides the increase of red cor-

pucles, an increase in the large lymphocyte element has been observed.

We have found this method of artificial lymphocytosis which brings with it some leucocytosis of value in other suppurations such as ear infections. It might prove of value in typhoid since the type of cells increased are similar to those increased in this disease.

It is possible that in the continued form of bone marrow hyperæmia other factors may influence the blood, such as oxidation products which may be retained longer than normally in the extremities.

Metchnikoff states that we are to accept it as a law that the leucocytes are capable of producing antibodies and that the microphages (polymorphonuclear leucocytes) must be regarded as the source of these protective substances in the blood and body fluids. However, he does not consider that they are secreted by the phagocytes. They are elaborated within these cells and are only capable of exerting any action after being set free, following the destruction of the cell—a process similar to that of the production of fibrin ferment due to the breaking down of leucocytes.

Using this conception of Metchnikoff's as a basis, Arneth[37] in 1904 published an exhaustive monograph on the behavior of the neutrophilic leucocytes in infectious diseases. He lays particular stress on the changes in the shape of the nuclei and divides the polymorphonuclear neutrophiles into five classes as follows:

Class I. Mononuclear neutrophiles.
Class II. Neutrophiles with 2 nuclei.
Class III. Neutrophiles with 3 nuclei.
Class IV. Neutrophiles with 4 nuclei.
Class V. Neutrophiles with 5 or more nuclei.

By averaging the counts on a number of normal individuals he finds the following percentages:

Class I.	Class II.	Class III.	Class IV.	Class V.
5%	35%	41%	17%	2%

While engaged in blood work we investigated the claims of Arneth with the results indicated in the following chart:

	One Nucleus.	Two Nuclei.	Three Nuclei.	Four Nuclei.	Five and more Nuclei.
Class I.—Normal Adults.					
55 Cases, 100 Counts.					
Average	8	36	42	13	1
Extremes	0–27	17–56	26–59	0.5–32	0–5
Mean	8	36	41	11	1
Arneth's Index: Average, 65; extremes, 50-86; mean, 67.					
Class II.—Cured Cases of Pulmonary Tuberculosis.					
58 Cases, 100 Counts.					
Average	8	39	40	12	1
Extremes	0–35	20–60	23–59	2–32	0–6
Mean	8	40	40	11	1
Arneth's Index: Average, 67; extremes, 29-88; mean, 67.					
Class III.—Improving Cases.					
38 Cases, 100 Counts.					
Average	10	41	39	9	1
Extremes	1.5–34	20–62	16–57	1–25	0–6
Mean	8.5	42	39	9	0.5
Arneth's Index: Average, 70.5; extremes, 47-91; mean, 71.					
Class IV.—Stationary Cases.					
37 Cases, 100 Counts.					
Average	15	41	39	4	1
Extremes	0.5–49	10–62	10–52	0.5–32	0–7
Mean	12.5	43	35	6	0.5
Arneth's Index: Average, 75.5; extremes, 31-94; mean, 78.					
Class V.—Advancing Cases.					
25 Cases, 100 Counts.					
Average	21.5	45	27	5.05	1
Extremes	2–50	10–62	10–51	0.5–37	0–11
Mean	20	49	28	4	0.3
Arneth's Index: Average, 80; extremes, 31-94; mean, 82.					

Arneth considers the cells in the higher classes, those with the more complicated nuclei, to be the riper and more efficient—the ones capable of producing the most antibodies.

Bushnell and Treuholtz[38] conceived from this blood picture an arbitrary index made by adding together the percentages in Class I and Class II and one-half that in Class III.

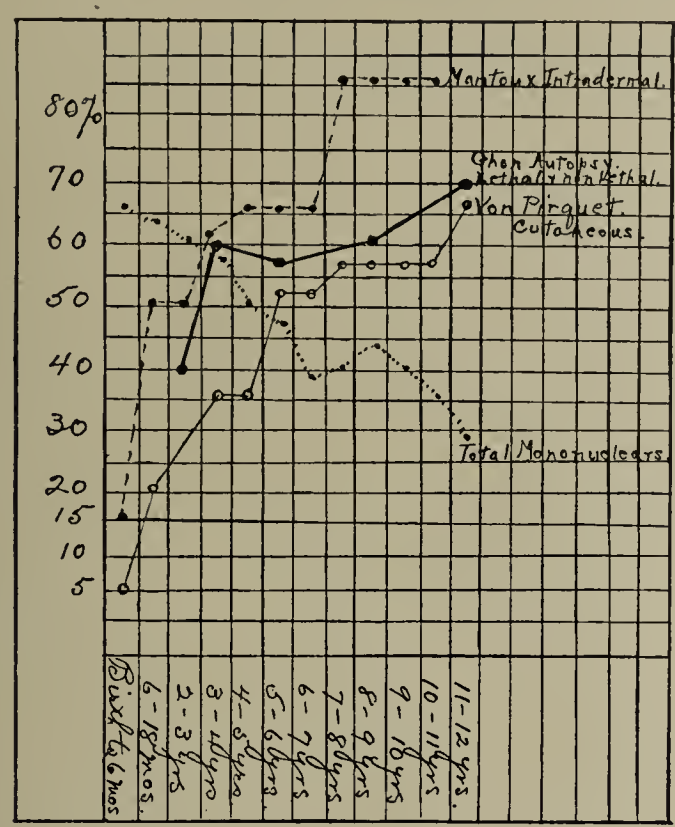
In studying the table we see that the averages of our counts in the various stages of pulmonary tuberculosis agree with the statements of Arneth; that, as a case progresses unfavorably, there is a decrease of the efficient cells, those in Classes III, IV and V, and an increase in the unripe cells, or those in Classes I and II.

Expressed in terms of Bushnell and Treuholtz's index, the higher the index, the lower the patient; but on closer scrutiny we note the great extremes in all the various stages. It is possible in the most advanced cases to get a blood picture whose index would be lower than the standard normal one, and among the normals to obtain one higher than the average for the most advanced cases. It is this extreme variability in the counts that has led us not to place too much value on isolated counts, though we do feel that a series of counts on a given patient gives us a certain idea as to the prognosis.

Diagnosis.

The following chart shows a great difference in the value of the cutaneous reaction and the intracutaneous reaction to tuberclin. It has been suggested that the intradermal test gives too many reactions, in other words, that non-tuberculous children and animals will react. But the chart also indicates that not so many children react to the von Pirquet test as autopsy records seem to require. It is extremely difficult when making repeated examinations to have children submit to the intradermal test. It is most important to make the most reliable test in children before and after submitting them to vaccination. It occurred to me, therefore,

to modify the "stick" reaction in the following manner, so that one can make an intradermal application of tuberculin with very little pain. We found that old tuberculin would dry on hypodermic needle points. These points are moistened with a drop of pure water placed on the sterilized skin and then plunged through the skin and given a twist as they are withdrawn. The reactions following this test are shown in the chart below. We have made about one hundred observa-



Note the drop in percentage of mononuclear cells or lymphocytes as age of child increases. As this occurs, the positive tuberculin reactions increase.

tions and we have found such tests positive when the von Pirquet test has been negative. The reaction is characterized by a definite lump, probably an actual tubercle. In two instances a slight temperature reaction followed this test. It is a test which children readily submit to repeatedly. The best location we find to be over the radial muscles, as here it is a very rare occurrence to puncture a vein, an incident which interferes with reaction.

It must be remembered too that children have a larger number of leucocytes than adults so that the change in absolute number of lymphocytes per cmm. from childhood to that of the adult would be a decrease from about 6000 per cmm. to about 3000 per cmm.

This occurrence may be of great importance in explaining the difference between tuberculosis in children and in adults.

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JOHN BELL, SURGEON. 1763-1820.

By Eugene R. Corson, M. D., Savannah, Ga.

"And gladly wolde he lerne, and gladly teche."

Read the writings of John Bell and you will see the greatness of the man and his nobility of character. Almost on every page you are aware of an intensity of conviction and a depth of feeling which come from a great mind and a great heart. I know no medical writer who is quite like him. His brilliant brother, Sir Charles, whose style charms you with its ingenuousness and warmth and color, is still very different. Generally speaking, the writers of a hundred years ago wrote in a way which seems to us stilted and formal beyond measure, and we weary of many pages. But John Bell has so much to tell us, and he is so anxious for his reader to know what he

has to teach, that his earnestness and his eagerness hold you, even when his argument is, perhaps, drawn out and he repeats himself. Sir Charles wrote as he was, simple, open-hearted, unaffected, with no rhetorical display, and yet with a nice use of words. You are aware that he writes to teach, but he is always more concerned with his own teachings than with the opinions of others, so that he is rarely polemical and never violent.

His brother John has also much to teach, but he is always concerned with the opinions of others; and when he sees their errors he will use every means to bring them out—the most incisive language, and even ridicule and sarcasm. Though usually dignified and most earnest, he may show humor, and even a broad humor which Sir Charles is inclined to apologize for. He is always the fighter, and the more prominent his antagonists the more ready he seems to attack. He never hesitates at high position, and is indifferent whether his antagonist is a contemporary or an old master in the profession. He brings out their errors, however, not simply to pick them out but to emphasize and teach what he regards as the truth. While free to censure he is equally free to praise, and he never omits an opportunity to show his admiration for the great Paré, or honest, bluff old Wiseman, or any old worthy, for that matter. Clearly as he has pictured for us the crudities of Frère Jacques, the savage jab of his dagger-knife, and his total ignorance of anatomy in the beginning of his work, he places him on a great pedestal in the Hall of Fame as the real originator of the modern operation of lithotomy, as one who cast to the winds the "apparatus major," and the perverted doctrine of Hippocrates that "wounds of membranous parts are mortal." But no matter what the subject, be it one in surgical pathology, or the application of a bandage, he writes with the same care and grace. And if his deeper nature be touched by the song of the nightingale, or by a scene in Florence by moonlight, he rises to the height of a fine impassioned prose.

John Bell came from good stock. His grandfather was a Mr. John Bell, minister of Gladsmuir, who was born on Feb. 2, 1676. He was noted for his industry, determination, and impressive eloquence, qualities all inherited by his grandson. He was called upon to preach the sermon on the death of William III before the General Assembly of the Church of Scotland. That he gained a reputation for a vigorous intellect before he was thirty shows him to have been a man of parts. He died at the early age of thirty-two, leaving several children, of whom William Bell alone comes into prominence as the father of four great sons, and as a member of the Catholic and Apostolic Church of Scotland. To have left the Presbyterian Church, of which his father and family were members, and to have become a minister of the Episcopal Church of Scotland, at a time when that church was under many restrictions and persecutions, shows his independence and fearlessness. His first wife, surviving all her children, died in 1750. In 1757 he married Margaret Morice, the elder daughter of an Episcopal clergyman. Early left an orphan, she was educated by her grandfather, Bishop White, afterwards Primus of Scotland. She was distinguished for her piety and many accomplishments, among which was a great talent for drawing which she transmitted to her children. She bore six children, of whom four sons rose to distinction, and even great distinction.[1]

Galton has found that the majority of men who reach eminence in science have had distinguished mothers, so that Charles and John Bell are no exceptions to the rule.

The eldest son, Robert, became an advocate and professor of conveyancing to the Society of Writers to the Signet, and was the author of the Scots Law Dictionary, and of several other works on the law of Scotland. He died in 1816. George Bell, the fourth son, was a distinguished jurist and professor of law in the University of Edinburgh. With the genius and distinction of Charles we are all familiar.

John was the second son, and was born on May 12, 1763, when his father was 59 years old. A month before his birth his father had been operated for stone, and his gratitude over his recovery led him to devote the talents of his son, born while he was convalescent, to the cause of medicine and to the benefit of mankind. Eleven years had to pass before the birth of his youngest son, Charles. Surely the operator in this case had much at stake, and his success deserved the perpetuation of his name, for at that time they had still much to learn of the operation, and the death rate was considerable.

John early showed his abilities. In the beginning he undoubtedly had the training of the home and the teaching of his distinguished mother, probably even more than Charles, who wrote so feelingly of his mother's influence and teaching. He was educated in the High School, and already showed a liking for medical studies. On entering the university he attended the lectures and practice of Black, Cullen, and Monro, Secundus, all famous names in the history of medicine. He was the special pupil of Mr. Alexander Wood, a prominent surgeon in Edinburgh. To him he dedicated the first volume of his Anatomy of the Human Body. While studying anatomy under the second Monro he conceived the idea of teaching the application of anatomy to surgery, a branch of instruction which Monro seems to have slighted. It became the dominant thought with him. He saw how the study of anatomy would dispel mere doctrines and hypotheses which did so much to retard the progress of medicine in all its branches. He saw the discipline which comes from the honest labor of dissection. As he writes in his preface:

> Of all the lessons which a young man entering upon our profession needs to learn, this is perhaps the first—that he should resist the fascinations of doctrines and hypotheses, till he has won the privilege of such studies by honest labor, and a faithful pursuit of real and useful knowledge. Of this knowledge, anatomy surely forms the greatest share. Anatomy, even when it is neglected, is universally acknowledged to be the very basis of all medical skill. It is by anatomy that the physician guesses at the seat, or causes, or consequences of any internal disease: without anatomy, the surgeon could not move one step in his great operations: and those theories could not even be conceived which so often usurp the

[1] See my paper on Sir Charles Bell. The Johns Hopkins Hospital Bulletin, 1910, XXI, 171.

place of that very science from which they should flow as probabilities and conjectures only, drawn from its store of facts.

In all his surgical writings this thought is ever uppermost. He taught it to his younger brother Charles, and when the latter published his Surgery he put on the title page "A System of Operative Surgery founded on the Basis of Anatomy." The value of this idea cannot be overestimated in the coming progress in surgery and the attainment of its present perfection. It was the first step. The second step came with anæsthesia, which permitted deliberate dissection of the living body; and the third step with Pasteur and Lister. I do not hesitate to place John and Charles Bell in line with these great names.

He must have graduated in 1785 or 1786, for in the latter year he became a Fellow of the Royal College of Surgeons of Edinburgh. Before beginning practice he traveled in Russia and the north of Europe. On his return he began at once to lecture on Anatomy and Surgery. In 1790 there was built for him a lecture theater in Surgeon's Square, where he gave regular courses of lectures and where he carried on his dissections and formed a museum. Until 1804, when his brother Charles went to London, he had his help as his demonstrator, as well as the use of his great artistic talent in the drawings of the dissections, and in the plates for publication. John Bell himself was no mean draughtsman, and he, too, etched or engraved many of his own drawings, as his works abundantly show. Charles, however, excelled him as an artist, though in artistic criticism John equalled, if he did not excell his brother. Charles' great System of Dissections, we must remember, was based on dissections made in his association with his brother. On several occasions Sir Charles refers to the critical and often severe tutelage of his brother. He speaks of him as his master, and in his annotated edition of the Surgery, published in 1826, he writes in the preface:

It is with great satisfaction that I present to the profession an edition of Mr. John Bell's works; and did it not sound like vanity, I would express a wish that the contents of these volumes may prove to the reader of the same value that the lessons of a brother have been to me.

But John Bell was not of a nature to live a peaceful and uneventful life, however much absorption in scientific work tends towards peace and happiness. He was too much concerned with the opinions of others. His love of truth made him eager to detect error wherever he could find it, irrespective of time, place, or person, and proclaim it from the housetops, and in language of no uncertain meaning. He was not in the university and could speak out and write as he pleased, his own master and independent. In his lectures on the surgery of tumors, addressed to his late pupils, the first discourse is headed by a quotation from Chaucer: "Full gladly would he learn and gladly teach" (*sic*). This well-known line applies most aptly to himself. He was as great a teacher as he was a great surgeon. He did not agree with Cicero that from the false there was no truth to be learned, but rather from our mistakes we learned the most. So he would pick out the errors as he saw them, of friends or foes, to emphasize his teachings. He did not hesitate to criticize severely Dr. Monro as an anatomist and Benjamin Bell as a surgeon, which brought down a storm upon him. In 1799 appeared a pamphlet entitled "Review of the Writings of John Bell, Esq., by Jonathan Dawplucker,"[2] which attempted to exonerate Monro and Benjamin Bell from his unfavorable criticism, and also attempted to show that the first volume of his Anatomy was a plagiarism. John Bell replied by publishing a second number of the Review under the same name of Jonathan Dawplucker, addressed to Benjamin Bell, with severe reflections on his System of Surgery. He vigorously attacked the stereotyped methods of both Monro and Benjamin Bell. He had the students with him, and the book lost its popularity.[3]

But this was only the gathering of a storm which was to last several years, and which was to draw Bell into a most bitter and lengthy controversy, demanding much of his time and energy, and undoubtedly of injury to his health.

Dr. James Gregory, the Professor of Physic in the university, who besides his great intellectual brilliancy, had behind him his father's reputation, and the momentum of inherited power, conceived the idea of excluding the younger members of the Royal College of Surgeons from practice in the Royal Infirmary, on the ground that the patients suffered from the constant changes in treatment in the monthly rotation of the surgeons. Bell fought the measure at every step. He appeared before the Board of the Infirmary and produced six folio books, filled with surgical drawings and cases, as evidence of his system of teaching and his need of clinical material; but they turned a deaf ear to him. He then brought the question before the Law Courts, whether they had the power to exclude him, and it was decided against him. Though Gregory carried his point he was subsequently severely censured by the Royal College of Physicians for violations of truth and unprofessional conduct.

Bell was appointed by the Royal College of Surgeons of Edinburgh to reply to the Memorial of Gregory, which he did in an octavo volume entitled "An Answer for the Junior Members of the Royal College of Surgeons of Edinburgh to

[2] The writer of this anonymous attack was undoubtedly Professor Gregory, himself. In John Bell's Letters on Professional Character, etc., addressed to Gregory, p. 64, he writes: "With all your equivocations about Dawplucker, I well knew that under that title you threatened my character."

[3] Referring to Gregory's first anonymous attack on him, under the name of Jonathan Dawplucker, and his reply under the same name, he wrote in his Letters on Professional Character, etc.:

"In the first number was reviewed one volume of Mr. John Bell's System of Anatomy. In the SECOND was reviewed, in like fashion, the SIX VOLUMES of Mr. Benjamin Bell's System of Surgery. The advertisement was of the same form and of the same size; it was stuck up on the same board, and on the same gates and sticking places with the first. But this, Sir, was not like the advertisement of your friends, a mere brutum fulmen: I neither mistook my bird nor missed my shot: down came the offensive advertisement, which had been renewed and carefully kept in the public eye for many weeks, and down came the SIX VOLUMES, the whole covey at one shot, and never a leaf has fluttered since."

the Memorial of Dr. James Gregory, on the Edinburgh Infirmary." This was published in 1800.

But the controversy did not end here. Ten years later he published a work entitled "Letters on Professional Character and Manners, on the Education of a Surgeon, and the Duties and Qualifications of a Physician, addressed to James Gregory, M. D., Edinburgh, 1810, 8vo." Thus did his grievance rankle long in his breast, to the detriment of his health and happiness, and to the detriment of our profession, which could ill afford to give up any of his time and energy to such an ignoble cause.

Evidently the Royal Infirmary was not on the lookout for either genius or talent, for it promptly turned down Charles Bell's proposal to pay the Hospital £100 a year, and to transfer to it the museum he had collected, on condition that he be "allowed to stand by the bodies when dissected in the theatre of the Infirmary, and to make notes and drawings of the diseased appearances."

This "Letters on Professional Character and Manners," etc. is indeed a most remarkable work, 636 pages of invective and righteous indignation, an expression of ten years of bitter controversy and professional strife. Gregory had seen fit in a quarto volume of 700 pages, full of scurrility and personal abuse, and even indecent jokes, to attack Bell and those junior surgeons whom he wished excluded from the Royal Infirmary. Copies of this work he had distributed gratis among friends and patients. He had even employed scurrilous handbills and posters distributed among the students and citizens generally. And to show him up to the world and to posterity Bell saw fit to write this book. Oh! the pity of it! that he should have been drawn into this strife! It was the great mistake of his life.

Brilliant as Gregory was and ever ready to quote his Virgil and Lucretius, he had an antagonist equally brilliant to answer him, and equally ready to quote from Latin literature and English literature, and to meet him on his own ground, and with his own weapons, and yet to be always the gentleman. Though Gregory gained his point, though he was the popular physician of the day and the brilliant lecturer in the university, and though fortune and prosperity followed him, I cannot accept Lord Cockburn's rather high estimate of his character. To me he seems mean and contemptible. He did no original work in science. He stands out a good example of mere intellectual brilliancy, as we use that term, without any abiding productiveness, or really contributing to anything.

It is a relief to pass from his polemical writings to his scientific works. The first volume of his Anatomy of the Human Body appeared in 1793, when he was thirty years old. In his preface he states very clearly his position in regard to anatomy and to his teachings to his students of this science, and in support of his position he quotes John Hunter, to whom he gives all praise as "the first anatomist and the truest physiologist of this or any age"; yet he does not hesitate to criticize him in his own peculiar way when differing from him. But not only in his Anatomy but in all his writings and teachings he tells his pupils to be an anatomist before being a physiologist, to study anatomy before taking up mere theories and hypotheses, and to be a good anatomist before attempting to operate upon the living body.

In 1794 appeared "Engravings explaining the Anatomy of the Bones, Muscles, and Joints, drawn and explained by the Author," quarto, Edinburgh. All the drawings and almost all the etchings and engravings are his own, sufficient evidence of his prodigious industry and labor. Volume II, on the Heart and Arteries, appeared in 1797, while Volume III, on the Brain and Nerves, the Organs of the Senses, and the Viscera, was the work almost wholly of Charles Bell. This Anatomy must stand in the history of medicine as one of the works which mark the progress of our science. If John Bell's drawings of dissections were sometimes rough, viewed from our standpoint to-day, they were honest drawings and no servile copies from other works, many of which had handed down from time immemorial the gross mistakes and fancies of copyists and imitators. Bell took pains to show many of these mistakes and their bearings on the grosser mistakes in surgery, especially as regards the surgery of the arteries. So far as I know he was one of the first who had a clear idea of the possibilities of the collateral circulation. The advances which were soon to follow in the surgery of the arteries, and especially in the surgical treatment of aneurism, of which he himself was a master, can truly be said to rest largely on his own anatomy of the blood-vessels. And I am not unmindful of the work of John Hunter, Sir Astley Cooper, and Abernethy in this branch. And when he came to apply this knowledge in his surgical discourses, it was to throw a flood of light upon the whole question. Looking back on these lectures after a quarter of a century, Sir Charles writes:

> In considering this admirable discourse, every one with the slightest tincture of science, or capacity for it, must be struck with the evidence it affords, and satisfied of its great importance to every branch of surgical practice.

The work was a popular one, went through several editions, and was translated into German when Germany was herself alive to anatomical study. In the preface to the first volume he states:

> I have endeavoured to make it so plain and simple as to be easily understood; I have avoided the tedious interlarding of technical terms (which has been so long the pride of anatomists, and the disgrace of their science) so that it may read smoothly, compared with the studied harshness, and, I may say, obscurity of anatomical description.

You see here the real love of the anatomist and the teacher.

In 1795 appeared his "Discourses on the Nature and Cure of Wounds." It seems strange to us to-day that it is not much over one hundred years ago that the profession was still largely influenced by the ancient notion that all wounds had "to mundify, incarn, and cicatrize," and that primary union was to be avoided as a dangerous shutting up of humors which had to be discharged. The opening sentence reads:

> When a modern surgeon allows himself to talk about the "mundifying, incarning, and cicatrizing of wounds," or directs how to "fill the wound up with good and sound flesh, and keep it to a fair and even level with the adjacent skin," he but proclaims his own ignorance of the properties of the living body.

Bell shows that the surgeon should strive to get primary union, that suppuration is a disease in itself, and that this primary union is obtained by smooth incisions, by as little disturbance of the tissues as possible, and a cut surface as free as possible from all oozing of blood, with the opposing surfaces carefully co-apted by adhesive strips and ligatures. He did not know what suppuration was, but he did know that too much disturbance and injuring of the tissues lead to suppuration. He was always careful not to close his incisions until all hæmorrhage had been controlled, and he writes of waiting fifteen minutes at times to assure himself that all oozing had ceased before he closed the wound. He writes:

This adhesion, then, is a property of the parts of the living body, which is perfect only while their structure is entire; which operates only where the opposite parts touch each other by the fullest contact, and sympathize with each other in their period and degree of action. It is interrupted if any foreign body be interposed; it is less perfect in every unhealthy condition of the system; but it is a property of which we are now so well assured, that we look for its good effects in the greatest, as well as in the smallest, wounds; and the union of a hare-lip, after it has been cut and pinned, represents the perfection of that cure which we attempt in every greater operation, and more confidently in every smaller wound; succeeding sometimes as perfectly after an amputation of the thigh, as after the most trivial wound of the cheek.

How clearly he has expressed himself!

Bell's chief contribution to medicine was his anatomy and pathology of the arteries, and their application to the surgical treatment of aneurism; and in his Discourse II on wounded arteries we see how carefully he had studied the whole subject. We see here his skill in ferreting out from the literature the clinical cases to illustrate his teachings, and how clearly he sees their errors and what these errors teach. We can see how much old French and mediæval and inelegant Latin he must have waded through to pick out this material for his use. As he himself wrote he is looking for facts, without any regard to the writers' opinions; and the surer he is of his facts, the less he thinks of their opinions. Many of these old descriptions of cases are very interesting reading. There was a more studied and more elaborate description given to the surroundings and conditions of the case than we are apt to use to-day, which added to the picturesqueness and vividness, while we give, rather, a long inventory of the symptoms without any attempt at local color or a background. Of course our vastly wider horizon has multiplied the details, but I believe we could add much to the attractiveness and impressiveness of our clinical cases if we thought more of the literary form and the local color.

Through these cases we get glimpses of the practice two or three hundred years ago, the crudities and barbarisms which had come down through the centuries almost unchanged, up to the time of grand old Paré, whom Bell takes every occasion to praise and whose enemies he puts to shame. The crude notions of, and ineffectual efforts at checking hæmorrhage up to the time of Paré, and for many years after, in fact, are brought out to show more clearly the only proper way of controlling hæmorrhage, namely, by enlarging the original wound, by a careful dissection and separation of the artery, and the application of the ligature. It was later, however, when he published his Surgery, that he developed more fully his ideas of the surgery of the arteries and of aneurism. In this second discourse he shows us an interesting little bit of history relative to the femoral artery and its profunda branch, and how this latter had been overlooked by many, and even by the great Heister, and misunderstood by Mr. Gooch and Professor Murray. As a great object lesson he gives a striking drawing of a dissection of the femoral with its profunda branch as a frontispiece to the book.

Though more elaborately developed in his Surgery he shows how wonderful the possibilities of the collateral circulation are, and how fully equal to almost all cases where the main trunk is tied or diseased. And to show this he gives us a long detailed description of a case of stricture of the aorta, and one of the ascending vena cava. It is in this discourse that he gives us the history of his operation for an aneurism of the posterior iliac artery (the posterior branch of the internal iliac) in the case of the poor leech-catcher, and I make no apology for quoting the entire case, not only to show his surgical qualities but also his fine descriptive powers:

A poor man, who was by trade a leech-catcher, fell as he was stepping out of a boat, and the long and pointed scissors which are used in his business being in his pocket, pierced his hip exactly over the place of the sciatic notch, where the great Iliac Artery comes out from the pelvis. The artery was struck with the point of the scissors, it bled furiously, the patient fainted; and in so narrow and deep a wound, the surgeon, when he came, found little difficulty in stopping it up, and less difficulty still in making it heal. The outward wound was cured; the great tumor soon formed; and the man traveled up from the North Country, where the accident had befallen him, and in six weeks after arriving in our hospital here with a prodigious tumor of the hip, his thigh rigidly contracted, the ham bended, the whole leg shrunk, cold and useless, as if it had been an aneurism on the fore part of the thigh.

The tumor was of a prodigious size, and by that very circumstance of its being one of the greatest aneurisms, it lost all the characteristics of aneurism; especially there was no pulsation, no retrocession of the blood when the tumor was pressed upon; there was nothing peculiar except this, that the great and sudden distension was the cause of great pain; and from the continual pain, lameness, and his hopes of a cure, he was ready to submit to anything, beseeching us to operate.

There was little doubt of its being a great aneurism, but there was a possibility of its being a vast abscess; and it was resolved, in consultation, that he should be carried into the operation room; that a small incision should be made; that the skin being cut, the bag itself should be just touched with the point of a lancet; and if found to contain matter should be fully opened; but if blood, that it was then to be considered as an aneurism of so particular a kind, as to entitle us to call for a full consultation.

I made an incision two inches and a half in length; the great fascia in the hip, blue, and very strong, formed the coat of the tumor, and under that were seen the big fibres of the great Glutæus Muscle. The knife was struck into it, and large clots of very firm black blood rolled out by the tenseness of the tumor, which began to emit the clots in this way the moment that it was opened at one point. There was one thing further desirable before we put the patient to bed, that we should understand the case so far as to be able to report to the consultation, whether the artery

was absolutely open, and whether it was the great artery of the hip. I continued, therefore (knowing that the opening I had made could be covered with the point of the thumb), to pull out a few more clots of blood, till the warm and florid blood began to flow; I then pushed in a tent-like compress into the small wound of the tumor (viz. of the fascia), laid a broad compress over the outward wound, and put the patient to bed with one of the pupils holding the hand upon his hip.

This was done at one o'clock, and at four the consultation met, and the operation was performed. And in my notes I find two steps of the operation chiefly marked: First: That upon our opening the tumor fully with an incision of eight inches long, and turning out the great clots, the blood was thrown out with a whishing noise, and with such impetus that the assistants were covered with it, and in a moment twenty hands were about the tumor, and the bag was filled with sponges, and cloths of all kinds, which had no better effect than the cloths which, in any accident, the friends in great confusion wrap round a wounded arm; for though the blood was not thrown in a full stream, nor in jets, it was seen rising above the edges of the incision; it floated by the sides of the cloths which were pressed down by the hands of the assistants. But we knew by a more alarming sign that the artery was throwing out blood; for the man, who was at first lying, not flat, but supporting himself on his elbows, fell down, his arms fell lifeless and without pulse over the side of the table, his head hung down and was livid, he uttered two or three heavy groans, and we believed him dead.

Secondly: Seeing in this critical moment that, if he was to be saved, it could be only by a sudden stroke, I ran the bistoury upwards and downwards, and at once made my incision two feet in length: I thrust my hand down to the bottom of the tumor, turned out the great sponge which was over the artery, felt the warm jet of blood, and placed the point of my finger upon the mouth of the artery; then I felt distinctly its pulse, and then only was I assured that the man was still alive. The assistants laid aside the edges of this prodigious bag, and sought out the several sponges which had been thrust in, and the bag being deliberately cleaned, and its edges held aside, I kept the forefinger of my left hand steady upon the artery, passed one of the largest needles round under my forefinger, so as to surround the artery: one of my friends tied the ligature, and then upon lifting the point of my finger, it was distinctly seen, that it was the Posterior Iliac Artery,—that the artery had been cut fairly across, and had bled with open mouth—that it was cut and tied exactly where it turns over the bone: and although the extremities were cold, the face of a leaden colour, and the man had ceased to groan, and lay as dead; though the faint pulsation could not be felt through the skin in any part of the body; we saw the artery beating so strongly, whenever I lifted my finger, that we were assured of our patient's safety; however, he was so low that, after laying down the sides of the sac, and putting bandages around the body to keep all firm, we were obliged to have a bed brought in, and having given him some cordials, we left him to sleep in the great operation room, attended by the pupils and by nurses.

This patient recovered though it took seven months to complete the cure. It is indeed worthy of republication and I trust another admirer of John Bell a hundred years hence will republish it. A great poem is an inspiration, and a great effort to save a human life is an inspiration; they both have the same source.

In all wounds of the arteries he urges the importance of enlarging the original wound, especially in punctured wounds, and picks out from the literature interesting cases showing the mistakes made by approaching the vessel by a new incision, though the usual route, and missing the punctured wound in the vessel. These clinical cases are analyzed with great skill and minuteness. It was a form of wound more common then when the practice of duelling was universal.

His discourse on gun-shot wounds was based on much practical experience. It will be remembered that his brother Charles went down to Portsmouth to study gun-shot wounds after the battle of Corunna, and later to Brussels after the battle of Waterloo for the same purpose. In 1798 John Bell visited Yarmouth to study gun-shot wounds among the seamen of Lord Duncan's fleet wounded at Camperdown. This led to his writing "A Memorial concerning the Present State of Military Surgery." He showed further his zeal in 1803 when Great Britain seemed threatened by an invasion of Napoleon, by offering his services to the government to form a corps of young men instructed in military surgery and the duties of the camp and hospital, with the view of their being helpful in the defense of the country. Like Sir Charles he was busy with his pencil and brush, and some of his drawings of the wounded adorn his System of Surgery. His proposal was first accepted but later declined as unnecessary.

Along the same lines he treats of wounds of the sword and bayonet, or any clean-cutting weapon, and then passes on to wounds of particular parts, the head, the breast, and the abdomen. He properly preferred enlarging the wound with the knife rather than with setons and tents, and could avoid making fun of Mr. Benjamin Bell for his use of these instruments.

He treats at length of wounds of the chest and lung, he saw the value of free incision and drainage in empyema, and understood thoroughly the value of a collapsed and non-functioning lung where there is an opening in the chest or there is fluid or air in the pleural cavity. His views of wounds of the peritoneum are interesting in the light of present-day advancement. He knew, of course, and quotes cases as examples, that many an apparently fatal wound of the abdomen is recovered from. He was fully aware that the abdominal cavity, so-called, was not a cavity. He writes:

Soldiers recover daily from the most desperate wounds; and the most likely reasons that we can assign for it are: The fullness of the abdomen, the universal, equable, and gentle pressure, and the active disposition of the peritoneum, ready to inflame with the slightest touch; the wounded intestine is, by the universal pressure, kept close to the external wound, and the peritoneum and the intestine are equally inclined to adhere; in a few hours that adhesion is begun which is to save the patient's life, and the lips of the wounded intestine are glued to the lips of the external wound.

It was on this reasoning that he advised but a single stitch for the intestine cut across:

The two ends of the gut may be made to adhere to each other; and the prudent way of favouring these adhesions is to introduce the one piece of intestine a little way within the other, and to make one single small stitch in that part of the circle which is farthest from the mesentery, and then draw the gut by means of that thread close up to the wound, and thus it will probably happen, that the mesentery will keep its side of the circle firm, that the stitch will keep the opposite side firm, that the gut being drawn by the thread, and pushed from behind and flattened by the universal pressure within the abdomen, the double adhesion may take place.

Benjamin Bell in his Surgery had advocated the complete stitching around of the intestine and so figured it in his work, and John Bell reproduces the figure alongside his own to contrast the two. He gives no cases to show he had ever employed this method. Benjamin Bell's plan, while it may in one way seem more surgical to us to-day, even with the conditions then existing, is quite impossible from another standpoint and is evidently a mere fancy. John Bell's, though it seems to show a timidity, must be ascribed rather to a constant tendency with him to simplify operations. He never feared large incisions, but he is ever warning his pupils against "piddling" work, as he inelegantly characterizes it. Later in his life, when the profession deprecated the radical operation of ovariotomy, he upheld it as a proper procedure, though there is no record of his having done the operation. After Ephraim McDowell, who was one of his pupils, had operated successfully, he sent his MS. to his preceptor for his perusal and approval, but he had already left for Italy, and the MS. was read by John Lizars, who was doing his work. This may explain how the latter was the first to follow in Houstoun's footsteps, for he did the operation successfully on Feb. 27, 1825, using the long ligature, which, by the way, was the ligature for the ovarian stump that John Bell's was for the intestine.

The idea prevailed for centuries that atmospheric air was noxious when introduced into the closed cavities of the body. It was prevalent one hundred years ago; and even after the introduction of antiseptics it was hard to dispel this notion, and the earlier antiseptic operations were done under the spray. Bell takes pains at some length to dispel this idea, and he does it in the strong language of his firm convictions.

His discourse on wounds of the head is admirable even in the light of to-day. It was to be further elaborated in his System of Surgery, where he introduced many interesting cases from the old masters to show the errors of the day and to teach the principles he thought correct. He draws for us fine clinical pictures differentiating concussion and compression and the indications for the trepan. He shows how this operation was abused, how they trepanned for everything, and with dreadful mortality; and not only once but many times in a wild effort to find something. He quotes the advice of Heister:

> In these cases it will be necessary to trepan first on the RIGHT side of the head, then on the LEFT side; afterwards upon the FOREHEAD, and lastly upon the OCCIPUT, and so *all round* until you meet with the seat of the disorder.

The last part of this work deals with dangerous wounds of the limbs and the question of amputation. He advises his students to read Le Dran, who says: "Wherever there plainly is a necessity for losing a limb, the sooner it is done the better"; and then to read Mr. Belguer, who exclaims: "To cut off a limb after a bad wound, what is it but to add wound to wound?" With rare judgment he points out the two sides of the question, enjoins his students to study each individual case freed from mere opinions.

> When your opinion is called for, pronounce it boldly; and say, if you think it right to say so, "This limb must be cut off." But when you are prevented by officious relatives, or if the patient should refuse his consent, when the accidents of the case interrupt you, or you are in a confused or dangerous camp, where operations cannot be done, then do what remains of your duty—not with the ill humor of a man thwarted in some little view, or smarting under the sense of a disappointment or affront—set yourself heartily and kindly to save your patient's limb and his life.

And he begins his last discourse: "The best operations are sometimes abused, and so is amputation abused: the most dangerous remedies are sometimes required, so is amputation." The whole chapter is clear thinking and good writing.

The first volume of the Principles of Surgery appeared in 1801, in quarto, with the title: "The Principles of Surgery, of the ordinary duties of the Surgeon; containing the Principles of Surgery as they relate to Wounds, Ulcers, and Fistulas; Aneurisms and Wounded Arteries; Fractures of the Limbs; and the Duties of the Military and Hospital Surgeon; with plates accurately colored from Nature."

The second volume appeared in 1806, "Containing the Operations of Surgery; viz., the Anatomy and Pathology of the Skull and Brain; in the form of Discourses on the Structure and Diseases of the Skull; the Structure and Diseases of the Brain; on Apoplexy, Palsy, Hydrocephalus, Phrenzy, the various species of Fractures of Skull and the Operation of Trepan."

The third volume appeared in 1807, being "Consultations and Operations on the more important Surgical Diseases, containing a Series of Cases calculated to illustrate chiefly the Doctrine of Tumors, and other irregular parts of Surgery: and to instruct the young surgeon how to form his prognosis and plan his operations. 37 Plates."

The work was popular and had a good sale in spite of its being expensive.[4]

In 1826 a new edition appeared under the supervision of Charles Bell in 4 Vols. 8vo. In the preface he writes:

> It has been my object in republishing these volumes, to retain all the important practical matter—to preserve, also, the admirable introductions, as well as the lively and ingenious illustrations. But in the original edition, the work was loaded with notes, containing long Latin quotations, and unnecessarily encumbered with excerpts from obsolete French works, ... I had long observed with regret that the admirable lessons contained in these works were to be got at with too much expense and labor, and that they were thus lost to the practising part of the profession.

The work to us is chiefly of value for its historical treatment of the principles it sets forth. Not only has there been a skillful use of clinical cases to illustrate these principles, but he has given us glimpses of the practices in the past. In his history of the doctrine of adhesion, for example, we have an interesting account of the professional suckers. No duel was complete without the presence of one such, who promptly

[4] In the publisher's advertisement we read: "The Principles of Surgery. By John Bell. In 3 volumes. Royal 4to. Illustrated with numerous engravings, many of them accurately colored from nature. Price £11, 11s. in boards, or each volume may be had separate. Vol. 1, price £4 4s. Vol. 2, £5 5s. Vol. 3, £2 2s."

sucked the punctured or incised wound, and applied a wad of chewed paper. The trade was not without its emoluments, for Verduc observed, "Suxerunt quidem, at non sanguinem sed potius aurum."

In the chapter on Hospital Gangrene, and, in fact, on many other occasions, we are shown the conditions existing in the great Hôtel Dieu at Paris. Bell called it "that great storehouse of corruption and disease," where this gangrene raged without intermission for two hundred years. "A young surgeon (says an ancient French author) who is bred in the Hôtel Dieu, may learn the various forms of incisions, operations, too, and the manner of dressing wounds; but the way of curing wounds he cannot learn. Every patient he takes in hand (do what he will) must die of gangrene."

The history of the treatment of hæmorrhage down to Paré, and the different methods of applying the ligature since his time, are well described. He thus leads up to his own views of the pathology and of the surgical treatment of wounded arteries and aneurisms, which form, I think, his greatest contribution to surgery. He taught the same great lessons in the surgery of the arteries which are taught to-day; that it must be a surgery founded on anatomy, that the collateral circulation is fully equal to the tying of any large arterial trunk; that the artery should be tied with the least disturbance of the surrounding tissues. While he fully appreciated the value of the Hunter operation, the technique of which he certainly improved upon, he saw that in the surgical treatment of aneurism there was a better method still, namely, to apply the tourniquet, lay open the aneurismal sac its entire length, dissect out the proximal end of the artery and tie it properly, avoiding other arteries and nerves in the ligature—then tie the distal opening—and "instead of merely cleaning away the great clots of blood, so as to see the wounded artery, we should wash and sponge it with particular care, fill it slightly with caddis or scraped lint, and compress it moderately with a general bandage." Even Sir Charles in his commentary twenty-five years later did not see that this was really an advance on the Hunter operation, for he wrote:

> But my master is here describing a circumscribed aneurism. .... You do not cut up a natural aneurism but tie the artery above it; so you may do here in a punctured artery, if the tumor be small and circumscribed.

John Bell really did and preached the Matas operation, lacking, of course, the asepsis, and the sewing up of the sac and wound as a natural sequence of the asepsis.

One point in the technique which he impressed upon his students with great emphasis, was not to trust to digital compression of the artery above the seat of operation—as stopping the pulse did not stop a dangerous flow of blood from the exposed or cut vessel—but to use the tourniquet.

In doing the Hunter operation he applied two ligatures and cut between, to allow each cut end to retract among the muscles, his idea being to imitate the tied artery in the stump of an amputation. He knew that there was less chance of secondary hæmorrhage from the stump of an amputation than from an artery tied in its continuity, and he explained it by the tied artery retracting among the muscles, which, by immediate cohesion or subsequent inflammatory exudate, helped to close permanently the vessel. He had tied most of the great vessels, the common carotid successfully, but failed on the external iliac, the man dying half an hour later from collateral hæmorrhage.

He devoted much space to the treatment of fractures, the nature of callus, and the vitality of bone itself, and you can see that bone was to him just as vital a tissue as the softer tissues. He pays most attention to fractures of the neck of the femur and of the patella, and differentiates in a very striking way between intra- and extra-capsular breaks, urging his pupils to base their pathology and treatment on the study of museum specimens. When Sir Charles published his beautifully illustrated work entitled "Observations on Injuries of the Spine and of the Thigh Bone," he wrote:

> Every question connected with the surgery of the thigh bone can be illustrated without going out of my museum, where there are thirty-seven examples of fracture of the body of the femur, independent of those of the neck; all these have been collected under the impulse given by my brother's impressive lessons on the importance of facts. I hope what I have delivered will convey to my hearers the same sentiments, and have with them a similar effect, teaching them to mistrust everything but anatomical proof.

Practically an entire volume is devoted to tumors, their nature and surgical treatment, with careful clinical descriptions of some of his own cases. He taught in no uncertain terms the importance of the removal of all tumors in the beginning of their growth. He gives a long discourse on the unlimited growth of tumors; on tumors of the bones; on tumors of the nostrils, gums, and throat, and especially on polypus. Some of his own cases of malignant growths of the parotid gland, lips, and cheek, operated on in a radical way, show fine dissection and surgical skill.

I know no separate work on the history of lithotomy and the development of the perineal operation as now done. Bell has written for us this history, covering two hundred and forty-eight pages, 8vo., and a clearer and more interesting chapter in the history of human endeavor I have never read. I could recommend any publisher to publish this history just as it stands. He has shown us how a great discovery may come to us from an humble source; that a great truth may find a ready acceptance with the unlearned, and meet its fiercest opposition with the "learned," as we use that term, and with those in high places. As he traces the modern operation back to Frère Jacques thus does he characterize him:

> Thus do we owe to this illiterate man, whose modesty, humility, and courage, whose charity, simplicity, and goodness, we must hold in respect, an operation which has been approved of, and performed by all the good lithotomists of Europe; and from his life and fortunes, one important lesson may be deduced; we may learn how slightly we should rely on our natural talents, how little faith we should have in mere courage!—this intrepid, fearless man committed nothing but butcheries, while he remained what has been termed a natural operator; but after having undergone the discipline of science, and learned the anatomy of the parts, he became truly valuable.

I have indicated Bell's controversial powers, and the constant tendency with him to fight for the truth as he saw it. I have tried to show as briefly as possible his great qualities as an anatomist, as a surgeon, and as a man of science. And now I would show another side of the man, in its way just as great, and more wonderful, perhaps, as so rarely seen coupled with high scientific attainments. I refer to his artistic talents and his love of the beautiful in nature and art. His brother Charles possessed this quality also, and while more skillful with the pencil, was, perhaps, less gifted as an art critic and interpreter of the beautiful; or, perhaps I should rather say, in his ability to give expression to the thought and the feeling when they mingle.

Early in 1816 he was thrown from his horse, which was the beginning of ill health which never left him. In 1817, with the hope of recovering his health and strength he started with his wife for Italy. Even at the beginning of his journey, before leaving Paris, he was evidently aware of the serious nature of his illness, for he had jotted down in his note-book, so full of fine observations on art and architecture:

> I have seen much of the disappointments of life. I shall not feel them long. Sickness in an awful and sudden form; loss of blood, in which I lay sinking for many hours, with the feeling of death long protracted, when I felt how painful it was not to come quite to life, yet not to die, a clamorous dream! tell that in no long time that must happen, which was lately so near.

And yet with this consciousness of the approaching end, he wrote out, with the same interest and industry he had written out his voluminous clinical records, his impressions of travel, and of the art and architecture of Italy which he had learned to love with all the ardor of the southern nature. In his youth he had enjoyed the wild scenery of his own land, and had shown a quick and delicate responsiveness to the beauties of nature. And now in this Italy of blue sky and sea, of the olive and the orange and the grape, with the glories of Greece and Rome still lingering, and with its own glories on every hand, he could forget his declining strength, and revel in the beauties about him. As we read these criticisms of the great masters, of the churches which the spirit of Christianity as well as the spirit of architecture itself had both wrought, we find a nature as sensitive, as clear to see the wonders of genius and the beauty of the flower by the roadside, as any real poet or true lover of the Earthly Paradise. If you will read his "Observations on Italy" you will see this lover of the Earthly Paradise, and his power to give expression to his love.

I cannot forbear quoting for you a page or two. He is wandering late in the night through a silent part of Florence, enjoying the solitude about him, and the great buildings in the moonlight, and thrilled by the occasional song of the nightingale, when he comes suddenly upon a procession of the Brethren of the Misericordia:

> Traversing the great centre of the city, along streets darkened from the height of the buildings, I passed along these immense edifices with strange feelings of solitude, as if in a dream, as if the gay and peopled world had vanished, and these gloomy mementos of the past alone remained. It was night, and in this distant spot not a soul was stirring, not a foot was heard, when, on crossing a narrow alley, the prospect suddenly opened, and the slanting rays of the full moon, falling with a softened light among the magnificent monuments of ancient times, displayed a splendid scene.
>
> At that moment the tower bell of the prison struck loud and long, tolling with a slow and swinging motion, seeming, from the effect of reverberation, to cover and fill the whole city; even in day this bell is distinguished from any I ever heard; but in the dead silence of the night it sounded full and solemn. Impressed by the feeling excited by the grandeur of the scene, I still prolonged my walk, and insensibly wandered on. The silence of night was unbroken, save by an occasional distant sound, arising from the busiest quarter of the city, or from time to time by the song of the nightingale, which reached me from the rich and beautiful gardens that skirt the walls of Florence, recalling to my mind the voice of that sweet bird, as I heard it when detained in the narrow valley of the gloomy Arco. I remember how its little song thrilled through the long melancholy of the night, a lengthened, oft-repeated note, which still came floating on the air like a light sleep. Involved in these musings of lulled and idle thought, I suddenly beheld in the distance, issuing from the portals of a large edifice, forms invested in black, bearing torches, which, casting a deepened shadow around, rendered their dark forms only dimly visible. Still increasing in numbers, as they emerged from the building, they advanced with almost inaudible steps, gliding along with slow and equal pace, like beings of another world, and recalling to mind all that we had heard or read of Italy, in the dark ages of mystery and superstition. As they approached, low and lengthened tones fell upon the ear; when the mournful chanting of the service of the dead told their melancholy and sacred office. The flame of the torches, scarcely fanned by the still air, flung a steady light on the bier which they bore, gleaming with partial glare on the glittering ornaments, that. according to the manner of this country, covered the pall.
>
> I looked with a long fixed gaze on the solemn scene, till, passing on in the distance, it disappeared, leaving a stream of light, which, lost by degrees in the darkness of night, seemed like a vision. The images presented to the mind had in them a grand and impressive simplicity, a mild and melancholy repose, which assimilated well with the hopes of a better world. It seemed like a dream, yet was the impression indelible.

Of the ordinary incidents of his life, and of those human qualities which had to do with his every-day life, I can gather but scant mention. In 1805 he married Rosina, daughter of a retired physician, Dr. Congleton. The marriage seems to have been a happy one, though childless like his brother Charles's. Mrs. Bell, five years after his death, published his notes on Italy, entitled "Observations on Italy." It was edited by his friend Bishop Sandford, of Edinburgh. A second edition appeared in 1835, with his additional notes on Naples. Mrs. Bell gives us a glimpse of his character in the preface. She writes:

> With warm affections and sanguine temper, he still looked forward with the hope that his labours and reputation would one day assuredly bring independence; and meanwhile, listening only to the dictates of an enthusiastic nature, and yielding to the impulse of feeling, he would readily give his last guinea, his time and his care, to any who required them. Judging of others by himself he was too confiding in friendship, and too careless in matters of business; consequently from the one he was exposed to disappointments, and from the other involved in difficulties and embarrassments which tinged the color of his whole life.

Although his income was large he seems to have lived in a style beyond his means. He lived at No. 9 George Street, at

that time a fashionable part of the new town of Edinburgh. He probably entertained much, for his musical parties were celebrated. His social gifts were many, especially his great conversational powers, with great learning, classical and artistic, and much general information. Sir Charles, in one of his letters to his brother George, referring to the life of his brother John, which he had written but decided, unfortunately, I think, not to publish, wrote:

He did dunch and press one; but since I lived with him I have scarcely enjoyed what may be called conversation.

I have failed to find any portrait or sketch of him. He is described as "below the middle height, of good figure, active looking, and dressed with excellent taste, keen and penetrating eyes gave effectiveness to his regular features, so that his expression was of a most highly intellectual type.[5]

There is a strange fascination which distance lends, be it of time or space, and we long to look closely at the great figures of the past to see exactly how they appeared. We long to touch something which they had touched, so that an autograph letter, or any little bit of personal belongings becomes quite priceless. So far I have failed to get anything to gratify this desire.

He died in Rome on April 15, 1820, dropsical and in great pain and suffering, and was buried in the Protestant cemetery. Sir Charles, in a letter dated June 4, 1840, wrote:

Went to poor John's grave. The Pyramid of Cestius attracts you from a distance. A plain stone marks the place as you enter the ancient reformed burying ground. A single antique column is between the enclosure and the pyramid. Remembering old times, a fitting resting place.[6]

Thus lived and died a great surgeon and a great man. He stood between the old medicine and the new; he saw the errors of the old, and helped prepare the way for the new. He was a worthy follower of John Hunter, for he taught a surgery on the basis of anatomy, and a pathological anatomy above all mere theories and opinions of disease; and last but not least, he taught a deliverance from mere authority and tradition by honest and ever vigilant investigation.

Nullius addictus jurare in verba magistri,
Quo me cunque rapit tempestas, deferor hospes.

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[6] In 1869 Sir James Y. Simpson visited the grave and had the stone repaired as a mark of his admiration.

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SOME SUGGESTIONS TO THOSE UPON WHOSE AID THE SUCCESS OF THE OPHTHALMIC SURGEON, IN CONSIDERABLE MEASURE, DEPENDS.*

By Samuel Theobald, M. D.,

Clinical Professor of Ophthalmology, Johns Hopkins University; Ophthalmic Surgeon to the Johns Hopkins Hospital, and to the Baltimore Eye, Ear and Throat Hospital.

However skilful the ophthalmic surgeon may be, the results of his work are materially influenced by the efficiency or lack of efficiency of those upon whose aid he must, in no inconsiderable measure, depend. An awkward surgical assistant, a nurse ill-trained or without aptitude may, with the best intention, perhaps, bring to naught his most painstaking efforts, and convert an operative procedure which otherwise would have been a success into a partial or complete failure. Every oculist who has operated extensively doubtless can recall such an experience. It has seemed to me, then, well worth while to offer some practical suggestions to those whose duty it is to supplement the work of the ophthalmologist.

The Surgical Assistant.—As of greatest importance, may be considered, first, the services of the surgical assistant. In many minor operations lack of skill or experience upon his part may be an inconvenience only; in other more important and delicate ones the success or failure of the operation may hinge upon it.

The assistant's first duty, it may be said, is to learn, for example, in "fixing" the eye, to keep his hands out of the operator's way. This is always practicable, and with a little study the art can easily be acquired. A steady hand, on his part, is also essential, and, if he will observe his chief, he will find that this is attained by resting the wrist or some part of the hand—the ring, or little, finger most probably—upon the patient's cheek or forehead. Few, if any, ophthalmic surgeons operate "from the shoulder." Again, if his fixation is to be satisfactory, he must grasp the conjunctiva—and a fairly broad grasp it should be—close to the corneal limbus, otherwise the loose conjunctiva will stretch, and the eye will not be held securely. If he is asked to rotate the eye in a certain direction, he must not simply *pull* it in this direction, but, bearing in mind the ball and socket-like movements of the eye resulting from the conjoint action of the straight and oblique muscles, he must really *rotate* it in the direction indicated. And in all such maneuvers, of course, he should be careful to exert a minimum amount of pressure upon the eyeball.

The sponging of an eye during a delicate operation, such as cataract extraction, deserves almost to be ranked as an art. For myself, I do not like dry sponging, but prefer the sponge should be dipped in a sterile boric solution, and then squeezed nearly dry before it is used. I also make it a rule, and I regard it as of real importance, that in such operations the assistant shall not sponge the eye unless he is directed to do so, and he is further cautioned to avoid, as far as may be practicable, bringing the sponge in contact with the cornea.

There is a certain maneuver, hard to describe, and, it would seem, not easily learned by the average assistant—perhaps, one might describe it as a momentary pressure followed by a gentle wipe—that is most effectual in removing coagulated blood from the conjunctival sac. It is often very helpful to the operator, and he is fortunate in having an assistant who has acquired the knack.

The elevation of the upper lid, in addition to that afforded by the speculum, in some cases facilitates the work of the surgeon. The assistant should do this with the forefinger, being careful to avoid pressing upon the eyeball. Another most helpful service he will occasionally be called upon to perform, is to exert counter-pressure upon the scleral margin of the section, to facilitate the extrusion of an obdurate cataract—one, perhaps, with an exceptionally large nucleus. In doing this he should gently depress the upper edge of the wound with a Daviel's curette, so as to cause the section to gape slightly, being careful that the instrument does not obstruct the exit of the lens; and when the lens is well engaged in the section, if called upon to do so, he may help to deliver it with the curette, by lifting or rotating its margin through the wound.

The assistant who can do all the things I have enumerated, just as the operator would have them done, if, perhaps, not worth quite his weight in gold, as the phrase runs, is, at all events, worth more than a score of helpers who can do them only in tolerable fashion.

The Nurse.—One of the most helpful advances in modern medicine and surgery, as all will agree, has been the providing of the trained nurse; but, until she has had very special training, she is not as helpful to the ophthalmologist as could be wished. For example, she has little appreciation of the delicacy of his instruments; she cannot understand, as I have learned to my sorrow, why a cataract or an iridectomy knife should not be put, loose, in the tray of an instrument case intended for forceps, needle-holders and artery clamps, or why his cutting instruments should not be boiled as long as his speculum or strabismus hook, or why they should not be boiled after, as well as before, an operation. A sponge is a sponge to her, and she fails to comprehend why the eye-surgeon makes such a pother about its size. In using an eye-dropper, she commonly holds it upside down, and she is as apt to place the candle, for oblique illumination, behind the patient's head as she is to hold it in front of it for an ophthalmoscopic examination.

She speaks of a fifty per cent solution of boracic acid, when she means a saturated solution which has been reduced to half this strength—about two per cent—by the addition of water; and, if the operator is so indiscreet as to permit her to wash and dry his cutting instruments, he, not improbably, will later

* A paper read before the American Ophthalmological Society, June 12, 1912.

realize his indiscretion. She offers to flood the room with sunlight for a first inspection after a cataract extraction, and wonders why he should prefer the dim light of a single candle, which she finally procures for him, after much diligent searching.

However, if she is reasonably intelligent and observing, and has had the advantage of a well-conducted training school, it will not require many weeks in an ophthalmic hospital to eliminate these particular shortcomings, and, assuming she is interested in the work, she will presently be as dependable and as helpful to the surgeon in her new field of labor as she was in the routine of the general hospital.

She will soon learn that the keen edge of a cataract knife will not stand more than thirty seconds' boiling, and that the slightest rough usage will blunt its delicate point; that the gauze needed to make a single sponge for the general surgeon suffices to make half a dozen or more for the ophthalmic surgeon; that the solution in an eye-dropper is apt to be contaminated if the dropper is held with its tip uppermost; that a candle flame in a moderately darkened room, with the help of a convex lens, affords a far more satisfactory view of the eye than any amount of diffuse daylight, and that the proper place to hold the candle for such an examination is a little in front of, and fifteen or twenty inches distant from, the eye to be inspected.

She will also learn, or should learn, that the important point with reference to the illumination of a ward or room in an ophthalmic hospital is that it should be *constant,* that, for example, a window-shade should not be allowed to be blown back and forth by the wind, so that at one moment sunlight floods the room, and at the next moment it is comparatively dark; that a painful eye is often made less so by elevation of the patient's head with an extra pillow or two; that, especially after a delicate operation, a patient with both eyes closed should never be permitted to take a single step without guidance; that the easiest way to drop a solution into an eye, and the way least perturbing to a nervous patient, is to draw the lower lid slightly away from the eye, while the patient throws his head back and looks upward, and let the drop fall into the space between the lower lid and the eye; that, if it is important the solution should come, undiluted, in contact with the cornea, the upper lid should be drawn up and away from the eye, while the patient, with his head thrown back, looks downward, the cornea being thus exposed, so that the drop may be made to fall directly upon it; that in employing poisonous collyria, as, for example, a strong solution of atropine or hyoscyanine, it is best to instil into the eye one or, at most, two drops, while with non-toxic solutions it usually does no harm, though it is wasteful, to apply more than two or three drops; that an eye-dropper, if it is to be used for more than one patient, should not be contaminated by permitting its point to come in contact with the lid margin or eyelashes, and that a dropper with which atropine or other mydriatic has been instilled should not be used presently to apply, for example, a zinc or boracic acid solution to the eye of another patient, if one would avoid causing the second patient several days of unnecessary inconvenience from mydriasis. And, finally, if she is exceptionally clever and painstaking, the neophyte may, some day, succeed in making, with absorbent cotton and a wooden toothpick, a mop which, without reconstructing it and, further, without doing violence to his conscience, the surgeon can use.

One of the most responsible duties falling to the lot of a nurse in an ophthalmic hospital is the cleaning and sterilization of an eye preparatory to an important operation. In doing this she should be, in the first place, most careful that the antiseptic solution employed is of the prescribed strength, for, if it is too strong, marked conjunctival injection, if not actual inflammation, may be induced, necessitating, possibly—as has happened in my experience—a postponement of the operation; while, on the other hand, if it is too weak, the sterilization may be ineffectual. In the next place, while she should be thorough in washing the lids and in flushing the eye with the antiseptic, she should, at the same time, be gentle in her manipulations, bearing in mind that the eye is an organ that resents rough usage. This admonition, it may be observed, applies with equal force to her care of an inflammation of the eye attended by copious discharge, in which frequent cleansing is called for, as in gonorrhœal conjunctivitis. Here, it is of the greatest importance that, in removing the discharge, she should be most careful not to abrade the corneal epithelium, since such a seemingly trivial traumatism may be the starting point of a destructive secondary infection of the cornea. And, in this connection, it may be further suggested to the neophytic ophthalmic nurse, and, perhaps, to some who hardly deserve to be so classified, that in the management of infectious diseases of the eye a thorough washing of the hands with soap and water, after contamination, is a much safer and more effectual measure than simply dipping them for a moment, as I have seen practised, in a bichloride solution.

The Apothecary.—A few suggestions to the apothecary, which I should be glad to feel might be heeded, seem to be called for.

First, I would entreat him never to dispense a so-called "safety" eye-dropper, the kind that has a flange-like affair near the tip, since it is an unmitigated nuisance, and distinctly less safe than the ordinary dropper. Secondly, I would suggest to him never to furnish, with a collyrium, a straight-pointed eye-dropper nor one that has a sharply curved tip. The dropper that is most useful is one that is not too long and has a slightly bent and not too slender tip. It will, if necessary, draw the last drop of the solution from the vial, which the straight one will not do, and it is less likely to catch in the neck of the vial and be broken than is the one that is sharply curved. Thirdly, I would ask him to dispense the ophthalmologist's much-prescribed yellow oxide of mercury ointment not in an opal glass box, now so much in favor, but in an amber-colored one, since this prevents the chemical action of light upon the mercury salt, and preserves the ointment much longer.

Finally, I would beg him—and this I do with many misgivings, knowing how difficult it is to uproot an old prejudice—to lay aside the mortar and pestle in preparing solutions of

readily soluble drugs, such as sulphate of atropine, and, instead, simply put the ingredients in a clean vial, insert an equally clean cork, give the vial a shake, and be satisfied. If he knew, as I do, how much more apt the mortar and pestle solution is to develop a fungous growth, after standing a week or two, than the one prepared in the simple manner suggested, he would, perhaps, be "almost persuaded."

It has been a matter of no little astonishment to me to learn recently from one of the most reliable apothecaries in Baltimore, and also from the dean of the College of Pharmacy connected with the University of Maryland, that they still uphold and teach the propriety of using the mortar and pestle in the manner indicated, without reference to the solubility of the drug prescribed. Certainly, in these days of asepsis and antisepsis, and of warring against contamination, the practice seems distinctly anachronistic.

To the *surgical instrument maker* I would say: When one's favorite cataract or iridectomy knife is sent to be sharpened, pray use only an oil-stone if possible. Do not *grind* it, if it can be avoided; for, when the "favorite" comes home, after the grinding process, its owner too often can hardly look upon it without recalling, sadly, Byron's lines

> Shrine of the mighty! can it be
> That this is all remains of thee?

I would also call his attention to a reprehensible tendency, which in recent years seems to have possessed his craft, to make the shanks of such instruments as canaliculus knives and strabismus hooks inordinately long, and to another, equally reprehensible, tendency, to give too sharp a curve to the blades of iridectomy scissors and of iris forceps. And, in this connection, I would make the further suggestion that an iridectomy knife is more completely under the control of the operator, and can be used with more deftness, if the angle between the shank and the blade is very obtuse—considerably more so than is usually the case with those made at the present day.

The Manufacturing Optician I would intreat never again to furnish cylindrical glasses, *with opaque sides,* in an oculist's trial case. There is no possible advantage in making the cylinders in this fashion, and there are two decided disadvantages. In testing cylindro-prismatic glasses which one has prescribed it not infrequently happens that the opaque portion of the cylinder must be placed just where it obstructs one's view, and so prevents an accurate determination of the strength of the prism. Again, if the cylinder, especially with its axis approximately horizontal, happens not to be carefully centered in the trial frame, there will be complaint from the patient that something, probably the upper opaque portion of the lens, is obstructing *his* view.

The American Optical Company, and probably other manufacturing concerns, make cylinders with the axis marked by two small, circular, white discs placed about 2 mm. from the edge of the lens, and with a line, more exactly indicating the axis, running from each disc to the metal rim. I have found these most satisfactory, and, it seems to me, they can hardly be improved upon.

The only other suggestion I have to offer is to emphasize the great importance of accurately centering trial-case lenses. This is not always done with the exactness that it might be, and the consequence is that errors are liable to occur in one's estimate of ocular muscle faults, and, confusion and contradictory results in neutralizing compound prescription glasses in which there is a prismatic element.

NOTES ON NEW BOOKS.

Public Health Chemistry and Bacteriology. A Handbook for D. P. H. students. By David McKail, M. D. (Glasg.), D. P. H. (Camb.), etc. Price 6/6. (*New York: William Wood & Co, 1912.*)

The author is modest in presenting this work to the public. He claims for it no originality, and offers it merely as lecture notes compiled from various standard works. It is a small octavo of about 400 pages, the first 150 devoted to chemistry, the remainder to bacteriology. Under chemistry he discusses chemical and water analysis, examination of air, soils, foods, beverages, disinfectants, antiseptics and deodorants; under bacteriology general principles, results of bacterial activity, immunity and anaphylaxis, micrococci, non-sporing and sporing bacilli, spirilla, spirochætes, yeasts and moulds, and special bacteriological examinations. There is a constant demand for these elementary handbooks and this one may be recommended with safety to students, who will find it a simple and easy book from which to gain the first principles of the subject but nothing more.

Operative Obstetrics Including the Surgery of the Newborn. By Edward P. Davis, M. D. Illustrated. $5.50. (*Philadelphia and London: W. B. Saunders Company, 1911*).

This book covering nearly 500 pages clearly demonstrates that the obstetrician of to-day must be a competent surgeon. Concise descriptions of the well-known procedures to effect delivery are given, but the most valuable part of the text relates to the more recent innovations in operative obstetrics such as pubiotomy and vaginal Caesarean section. The author has taken the pains to collect the results of these operations as published to date. Those who advocate the operations have been quoted extensively but the various objections raised against them are also given. The advice offered with regard to their value is conservative, but no more so, perhaps, than is justified by the relatively short period of time in which there has been opportunity to test their usefulness and learn their limitations. It is disappointing to find the lateral posture recommended for the performance of forceps operations. The practical character of the book will increase its popularity; the illustrations, of which there are 264, will prove most helpful to those who have not had the opportunity to witness the performance of the operations. It is a hopeful sign of progress in American text-books to find bibliographies, such as are here given; they are certain to stimulate students and practitioners to consult original sources.

Oxford Medical Publications: Common Disorders and Diseases of Childhood. By George Frederick Still, M. A., M. D., etc. Second edition. $5.50. (*London: Henry Frowde and Hodder & Stroughton, 1912*).

The new appearance of this book only increases our appreciation of it, which was expressed in our issue of December, 1911. The author has written an excellent work; he does not, as his

title indicates, endeavor to cover *all* the diseases of children, but only the commoner ones with which he has had a large experience, and these are the ones that the general practitioner meets with and wants to know how to treat. If he studies Still's work, he will be well guided. We wish that other authors would follow in Still's footsteps, and write rather on the diseases they are constantly seeing than on diseases which are practically unknown to them. Many of the treatises on medicine, surgery, etc., are poor because the authors attempt too much, not having had the necessary experience to write comprehensive works. The modifications of this second edition add to its value, and we commend the work heartily once again to the medical profession.

BOOKS RECEIVED.

The Treatment of Shortsight. By Prof. Dr. J. Hirschberg. Translated by G. Lindsay Johnson, M. D., F. R. C. S. With twelve illustrations. [1912.] 12°. 123 pages. Rebman Company, New York.

A Textbook of Ophthalmology. In the Form of Clinical Lectures. By Dr. Paul Roemer. Translated by Dr. Matthias Lanckton Foster. With one hundred and eighty-six illustrations in the text and thirteen colored plates. Volume I. [1912.] 4to. 275 pages. Rebman Company, New York.

Fourth Report of the Wellcome Tropical Research Laboratories at the Gordon Memorial College, Khartoum. Volume B.—General Science. Andrew Balfour, M. D., B. Sc., F. R. C. P. Edin., D. P. H. Camb., Director. 1911. 4to. 333 pages. Published for Department of Education, Sudan Government, Khartoum, by Baillière, Tindall & Cox, London; Toga Publishing Company, New York.

A Surgical Treatment of Locomotor Ataxia. By L. N. Denslow, M. D. 1912. 12mo. 118 pages. Baillière, Tindall and Cox, London.

United States. Treasury Department. Public Health and Marine Hospital Service. Annual Report of the Surgeon General of the Public Health and Marine Hospital Service of the United States. For the Fiscal Year 1911. 8vo. 331 pages. 1912. Government Printing Office, Washington.

Immunity. Methods of Diagnosis and Therapy and their Practical Application. By Dr. Julius Citron. Translated from the German and edited by A. L. Garbat. Twenty-seven illustrations, two colored plates and eight charts. 1912. 8vo. 209 pages. P. Blakiston's Son & Co., Philadelphia.

La Vie et les Maladies du Sang. Par le Dr. G. Froin. 1911. 8vo. 240 pages. G. Steinheil, Paris.

Les Otites Moyennes et Leurs Complications. Par Pierre Descomps et Paul Gibert. Avec une préface de P. Sebileau. 1912. 8vo. 256 pages. G. Steinheil, Paris.

Transactions of the College of Physicians of Philadelphia. Third Series. Volume the Thirty-third. 1911. 8vo. 416 pages. Printed for the College, Philadelphia.

A Cyclopedia of American Medical Biography. Comprising the Lives of Eminent Deceased Physicians and Surgeons from 1610 to 1910. By Howard A. Kelly, M. D. Illustrated with Portraits. Two Volumes. 1912. 8vo. W. B. Saunders Company, Philadelphia and London.

State Board of Health of the State of Ohio. Twenty-fifth Annual Report for the Year Ending December 31, 1910. 8vo. 410 pages. 1911. Columbus, Ohio.

National Association for the Study and Education of Exceptional Children. Proceedings of the Second Annual Conference on the Problem of the Exceptional Child. December 1-2, 1911. 8vo. 190 pages. Richard G. Badger, Boston, Mass.

Kystes Hydatiques du Poumon. Par Pedro Escudero. 1912. 8vo. 270 pages. G. Steinheil, Paris.

An Index of Differential Diagnosis of Main Symptoms. By Various Writers. Edited by Herbert French, M. A., M. D., Oxon., F. R. C. P., Lond. With sixteen colored plates and over two hundred illustrations in the text. 1912. 8vo. 1017 pages. John Wright & Sons, Ltd., Bristol; Simpkin, Marshall, Hamilton, Kent & Co., Ltd., William Wood & Co., New York.

The Medical Annual. A Year Book of Treatment and Practitioner's Index. Thirtieth Year. 1912. 8vo. 887 pages. John Wright & Sons, Ltd., Bristol; Simpkin, Marshall, Hamilton, Kent & Co., Ltd., London.

The Prevention of Dental Caries. By J. Sim Wallace, D. Sc., M. D., L. D. S. Second edition. 1912. 8vo. 67 pages. Office of the Dental Record, London.

Surgery of Deformities of the Face, Including Cleft Palate. By John B. Roberts, A. M., M. D. Illustrated with 273 figures. 1912. 8vo. 273 pages. William Wood & Company, New York.

Diagnose und Therapie der Magen- und Darmkrankheiten. Anhang: Die chemische und mikroskopische Untersuchung des Mageninhaltes und der Fæces. Von Privatdozenten Dr. Walter Zweig. Zweite, vermehrte Auflage. Mit 36 Textabbildungen und 1 farbigen Tafel. 1912. 4to. 502 pages. Urban & Schwarzenberg, Berlin & Wien; Rebman Company, New York.

Nervöse Angstzustände und ihre Behandlung. Von Dr. Wilhelm Stekel. Mit einem Vorwort von Professor Dr. Siegmund Freud. Zweite, vermehrte und verbesserte Auflage. 1912 4to. 448 pages. Urban & Schwarzenberg, Berlin & Wien; Rebman Company, New York.

On Bronchial Asthma. Its Pathology and Treatment. By J. B. Berkart, M. D. Revised and abridged third edition. 1911. 8vo. 150 pages. Henry Frowde, Oxford University Press, London, Edinburgh, New York, Toronto and Melbourne.

Lateral Curvature of the Spine and Round Shoulders. By Robert W. Lovett, M. D. Second edition, revised and enlarged with 171 illustrations. 1912. 8vo. 192 pages. P. Blackiston's Son & Co., Philadelphia.

A Manual of Surgical Treatment. By Sir W. Watson Cheyne, Bart., C. B., D. Sc., LL. D., F. R. C. S., F. R. S. and F. F. Burghard, M. S. (Lond.), F. R. C. S. New Edition. Entirely revised and largely rewritten with the assistance of T. P. Legg, M. S. (Lond.), F. R. C. S. and Arthur Edmunds, M. S. (Lond.), F. R. C. S. In Five Volumes. Volume II. 1912. 8vo. 570 pages. Lea & Febiger, Philadelphia and New York.

The Ocular Muscles. A Practical Handbook on the Muscular Anomalies of the Eye. By Howard F. Hansell, A. M., M. D., and Wendell Reber, M. D. Second edition, rewritten, enlarged. With 3 plates and 82 other illustrations. 1912. 8vo. 223 pages. P. Blackiston's Son & Co., Philadelphia.

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BULLETIN

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HEXAMETHYLENAMIN IN THE TREATMENT OF SYSTEMIC INFECTIONS WITH A SPECIAL EMPHASIS UPON ITS USE AS A PROPHYLACTIC.

By S. J. Crowe, M. D.,

Externe in Surgery, The Johns Hopkins Hospital.

The suggestion that hexamethylenamin be used in the treatment of systemic infections is based entirely on the results of experimental and clinical observations; and the object of this publication is to call attention to the fact that this drug is of value, not only as a therapeutic, but especially as a prophylactic measure, in a great variety of maladies. Among the conditions which may be favorably influenced by the administration of hexamethylenamin, the following are the most important:

(1) Infections of the genito-urinary tract and typhoid bacilluria.

(2) Infections of the bile ducts and gall bladder.

(3) Infections of the cerebro-spinal system, poliomyelitis, epidemic meningitis, meningeal infections following injuries or infectious processes elsewhere in the body.

(4) Infections of the respiratory tract, including infections of the para-nasal sinuses and ears, acute rhinitis, acute tonsillitis, and some forms of bronchitis. (In lobar pneumonia and pulmonary tuberculosis it is doubtful whether this drug is of any value.)

Hexamethylenamin, itself, is well known to practitioners in all parts of the world as the best of the genito-urinary antiseptics. It is sold under various proprietary names; such as, urotropin, helmitol, cystogen, formin, uratone, etc.[1] Hexamethylenamin is prepared by the action of formaldehyde on ammonia, and owes its value as a therapeutic agent to the fact that it undergoes decomposition in the body liberating free formaldehyde. This fact was first noted in 1895 by Nicolaier.[2] After the administration of hexamethylenamin (urotropin) in doses of three to six grams (45 to 60 grains) a day, Nicolaier found that this drug, or its decomposition product formaldehyde, invariably appears in the urine in amounts which suffice to markedly inhibit the growth of organisms—even when a voided specimen of urine is directly inoculated (with streptococcus) and kept under the most favorable cultural conditions. In 1898, Richardson[3] called attention to the fact that post-typhoid bacilluria may be prevented by the daily administration of small amounts of hexamethylenamin throughout the course of typhoid fever.

[1] Although certain of these preparations are less irritant, there are none which liberate more formaldehyde than does the chemically pure hexamethylenamin.

[2] Nicolaier: Deutsche med. Wchnschr., 1895, XXI, 541-543; Deutsches Arch. f. klin. Med., 1904, LXXXI, 181-223.

[3] Richardson: J. Exp. M., 1899, IV, 19.

Further investigations, however, concerning the pharmacology of hexamethylenamin, were not made until 1908; in this year some experimental studies,[4] carried out in the pharmacological laboratory of the Johns Hopkins University, disclosed the fact that this drug is not excreted by the kidneys alone, but that within a short time after its administration by mouth it may be demonstrated in practically *all* of the body fluids.

The presence of hexamethylenamin, or formaldehyde, in a given secretion may be quickly determined by a simple chemical test.[5] By employing this test it was found that hexamethylenamin is invariably excreted into the bile, pancreatic juice, cerebro-spinal fluid, saliva and milk. It may also be demonstrated in synovial, pleural and peritoneal effusions, and in the circulating blood. It finds its way into the bile both through the liver and through the wall of the gall-bladder, as may be shown by administrating the drug to an animal after a preliminary ligation of the cystic duct, and testing separately the bile escaping through the common duct and that contained in the gall-bladder. Aside from the single, isolated observation of Bucura,[6] in 1907, that hexamethylenamin is excreted in the milk, it had not been recognized that this drug appeared in any of the body fluids other than the urine and circulating blood.

Following our experimental studies in 1908, some investigations made on clinical cases, in which it was possible, due to the presence of a post-operative biliary fistula, to make cultures and obtain specimens of bile directly from the interior of the gall-bladder, disclosed the following facts:

(1) Hexamethylenamin, given either by mouth or by rectum, makes its appearance in the bile and in the urine almost simultaneously.

[4] Crowe: Johns Hopkins Hosp. Bull., 1908, XIX, 109. Arch. Internat. de Pharmacodyn. et de Thérap., 1908, XVIII, 315.

[5] Hexamethylenamin undergoes decomposition so readily that it may be said to respond to all the formaldehyde tests with which we are acquainted. By the well-known reaction with bromine water (tetrabromhexamethylenamin appears as a precipitate), it is easy to demonstrate the presence of hexamethylenamin in a given excretion, but this test throws no light whatever on the presence of formaldehyde. The modified Hehner's test has proven to be the most satisfactory, although it is purely a formaldehyde test. Formaldehyde is liberated by the catalytic action of sulphuric acid on hexamethylenamin, and in the presence of a small amount of casein a deep amethyst color is developed. In clear solutions, such as the urine, pancreatic juice and cerebro-spinal fluid, or by using the distillates of bile or purulent effusions, the approximate concentration of the drug may be determined by comparing the color with that given by a formaldehyde solution of known strength. The method of applying the test is as follows: To the colorless fluid to be tested a drop or so of milk or a very small amount of casein is added, and this mixture stratified with an equal volume of the reagent, which is composed of 100 cc. of 99 per cent sulphuric acid and one drop of a 3 per cent ferric chloride solution. A deep amethyst color develops at the juncture of the layers and may be diffused by shaking. If formaldehyde (hexamethylenamin) is present in too great a concentration, however, the color reaction may not occur without dilution of the fluid.

[6] Bucura: Ztschr. f. exp. Path. u. Ther., 1907, IV, 398.

(2) Provided large doses of hexamethylenamin are given, at least 75 grains a day, this drug appears in the gall-bladder in a concentration which suffices to render the bile an unsuitable media for the growth of bacteria.

In some of the cases, in which the infecting organism was *B. typhosus,* it was possible, by the simple administration of hexamethylenamin, to render the interior of the gall-bladder sterile—at least so long as active therapy was continued. These results led us to conclude that hexamethylenamin would be of great value in the prevention and treatment of acute infections of the bile passages, and that it should always be given as a protective measure before operations on the gall-bladder or bile ducts.

Since it has been repeatedly shown that the spread of typhoid fever is largely due to infected excretions, and that the relapses occurring during the course of this disease are due to some locally persisting infection, not infrequently situated in the gall-bladder, we strongly recommend that large doses of hexamethylenamin be given throughout the course of typhoid fever as a prophylactic measure. As will be shown in discussing the toxicity of hexamethylenamin, this drug has, in the majority of cases, no untoward effects if given in small doses, at frequent intervals, and sufficiently diluted with liquids.

Our investigations during the past four years have been chiefly directed toward the experimental and clinical study of the value of hexamethylenamin in threatened or actual cerebro-spinal infections. There are a great variety of conditions, such as compound fracture of the skull (especially if the fissure passes through the middle ear or cribriform plate), infections of the scalp, acute infections of the ear or accessory nasal sinuses, or certain operative procedures which may be followed by an infection of the cranial cavity, in which it is especially desirable to have some measure for combating a secondary infection of the meninges. Also the number of reported cases of intra-cranial complications—meningitis, abscess and sinus thrombosis—which have followed a primary inflammatory process in the nasal cavities or para-nasal sinuses, now form an extensive series. Moreover, it has been shown by Flexner, and others, that both the meningococcus and the virus of poliomyelitis appear to have a predilection for invasion of the mucous membrane of the naso-pharynx, and from there to pass, presumably by the lymphatics, to the central nervous system. Post mortem studies in poliomyelitis, however, have shown that in both the experimental and the epidemic cases there is always an inflammatory reaction of the meninges preceding the invasion of the nervous system; thus holding out some hope that when the early symptoms of this disease are recognized, its further progress may be arrested by the administration of a drug which will be excreted into the cerebro-spinal fluid, and so render this fluid an unsuitable media for the continued growth of the virus.

That hexamethylenamin might actually be of value in the prevention and treatment of meningeal infections was first suggested to me by Dr. Harvey Cushing. This supposition was

confirmed by some experimental observations,[7] made in 1909, from which the following conclusions may be drawn:

(1) Hexamethylenamin, given either by mouth or by rectum, invariably appears in the cerebro-spinal fluid, both in man and in animals.[8] By comparative chemical tests it was determined that the concentration of hexamethylenamin in the cerebro-spinal fluid reaches its height from thirty minutes to an hour after its administration. This point is of the greatest practical importance in determining the frequency with which this drug should be given in cases with a meningeal infection, and will be fully discussed in a later section.

(2) After doses of hexamethylenamin, within therapeutic limits, a sufficient amount of the drug appears in the cerebro-spinal fluid to have a marked inhibiting effect on the growth of organisms (streptococcus) inoculated into this fluid after its removal from the body.

(3) Following a subdural inoculation of dogs and rabbits with a virulent culture of streptococcus, sixty to eighty grains of hexamethylenamin a day, given under conditions which insure absorption, will markedly defer, and in some cases prevent the onset of a fatal meningitis. This conclusion is based on the results of forty experimental observations. In each experiment four animals were used. The dura in each animal was exposed, under aseptic precautions, by a trephine opening in the broad posterior arch of the atlas, and 0.1 cc. of a boullion culture of streptococcus was injected into the cerebro-spinal space. One animal in each experiment was used as a control; the other three receiving hexamethylenamin under varying conditions and in varying amounts. In no case did the control animal survive longer than thirty-six hours, and on examination a diffuse, purulent meningitis was found; in many of the others the progress of the infection was held in abeyance during the continuance of active therapy, but as soon as the drug was withdrawn the organisms immediately began to multiply, with a return of clinical symptoms.[9] A few of our animals, however, made a complete recovery after a prolonged and careful treatment; and at autopsy, several weeks later, no trace of an infection could be seen, other than a slight thickening of the meninges near the point of inoculation. It is worthy of note that the only animals which recovered after a direct subdural inoculation were those to whom large doses of hexamethylenamin were given, as a *prophylactic* measure, for several days preceding the inoculation.

[7] Crowe: Johns Hopkins Hosp. Bull., 1909, XX, 102.

[8] From a pharmacological standpoint it is interesting to note that hexamethylenamin is the only substance known which is excreted into the cerebro-spinal fluid in amounts sufficient to be of the slightest therapeutic value. Of the inorganic substances, the bromides, mercury and lead do not appear in the cerebro-spinal fluid; potassium iodide, lithium and thallium have been found in very minute traces. Of the organic substances, traces of acetone have been found in the cerebro-spinal fluid of severe cases of diabetes with acetonuria; also chloroform may appear in minute quantities after a prolonged anæsthetization. Salicylic acid compounds are not excreted in the cerebro-spinal fluid. Bile pigments and dyes, with the exception of pyrrol-blue, and many of the toxins and immune bodies present in the blood serum may not be demonstrated in the cerebro-spinal fluid. Urotropin, however, invariably appears, and after therapeutic doses, in man, has been found in a concentration of 5 cg. to the liter. (Hald: Arch. f. exper. Path. u. Pharm., 1911, LXIV, 329.) This also furnishes a good example of the specific properties of endothelium.

[9] This is much the same experience that has long been had with hexamethylenamin in the treatment of genito-urinary infections, and we have had a similar outcome in two clinical cases of meningitis in which it was necessary, on account of the bladder irritation and hematuria, to withdraw the drug.

Clinical Experiences.

Since 1908, it has been a routine measure in the Johns Hopkins Hospital to administer hexamethylenamin to all cases in which a meningeal infection is a possible or threatened complication. Quite an extensive series of such cases have been studied during the past three years, and the results seem to definitely establish the therapeutic and prophylactic importance of this drug. This series includes cases of:

(1) Compound fracture of the skull.

(2) Tumors of the hypophysis with neighborhood symptoms necessitating operative procedures through the nose.

(3) Post-operative cerebro-spinal fistulæ.

(4) Infections of the ear and para-nasal sinuses.

(5) Acute poliomyelitis.

Fractures of the Skull.

The serious nature of compound fractures of the skull lies not only in the possibility of an intracranial bleeding, but in the extreme likelihood of infectious meningitis or cerebral abscess following the inoculation of septic material. As a rule, fractures of the base are attended with a higher mortality than are those of the vault, since an insignificant fissure which passes across the ethmoid plate may open a pathway of infection from the nasal cavity. Not infrequently a rapidly fatal pneumococcal meningitis may start up on the third or fourth day after what appears to be a simple, uncomplicated basal fracture with but few, if any, subjective symptoms.

With the hope of preventing complications of this character, we have, during the past three years, given hexamethylenamin as a routine measure to all patients admitted to this hospital with an injury of the head. There have been thirty-five consecutive cases of undoubted basal fracture, with bleeding, or escape of cerebro-spinal fluid from the nostrils or ears, without a single instance of a secondary meningeal infection.[10] There were, however, nine deaths ascribed to meningeal infection or brain abscess among the thirty-five earlier cases of basal fracture to whom hexamethylenamin was not given.

During the past five years there have been twenty cases of compound fracture of the vault, similar, in that there was a laceration of the meninges and underlying cortex in each in-

[10] Many of these patients are unconscious when brought to the hospital, others have nausea and vomiting to such a marked degree that it is inadvisable to give liquids by mouth; in these cases the hexamethylenamin is administered per rectum, from thirty to sixty grains being dissolved in 300 cc. of salt solution, or plain tap water, and allowed to slowly flow into the bowel.

stance. In eight of the earlier cases hexamethylenamin was not given and the mortality from infection was fifty per cent.[11] To each of the remaining twelve cases, hexamethylenamin was given immediately after the injury, and at frequent intervals until all danger of infection was past; ten of these patients recovered, while two succumbed with a pneumococcal meningitis.

In one of these fatal cases there was an extensive depressed fracture of the skull and foreign matter had penetrated far into the cortex. At operation the wound was cleansed as well as possible and adequate drainage established. For ten days the symptoms of an intracranial infection were held in abeyance by the administration of from 120 to 140 grains of hexamethylenamin a day. At the end of this time, however, it was necessary to temporarily withdraw the drug on account of painful micturition and hematuria.[12] The general condition of the patient rapidly became worse and death occurred thirty-six hours later; the autopsy disclosed a diffuse, suppurative meningitis. We have several times had a similar experience with hexamethylenamin in experimentally produced cerebral infections in animals; and it is well known that in chronic infections of the urinary bladder the symptoms may temporarily subside, but tend to reappear soon after the inhibiting influence of the drug has been removed.

Although it is difficult to ascribe the recovery in an individual case to any particular form of therapy, still in view of our experimental observations, it seems justifiable to give the following histories, as examples of the prophylactic and therapeutic value of hexamethylenamin in meningeal infections.

Compound Fracture of the Skull; Cerebro-spinal Rhinorrhœa for 25 days; Recovery. Average amount of Hexamethylenamin 70 grains a day (for 28 days); no toxic effects.

Surgical No. 23467. F. L., a laborer, 30 years of age, was brought to the Johns Hopkins Hospital, on January 15, 1909, in an unconscious condition. About two hours before admission he had fallen from a travelling crane into a pile of scrap-iron twenty feet below. There was a large, jagged wound running from the right temporal region into the external canthus and across the right upper lid to the root of the nose. Through the center of this dirty wound, which had been bleeding profusely, there was a constant oozing of cerebro-spinal fluid and fragments of cortex. At operation the wounds were cleansed as well as possible, the bleeding controlled and protective drains inserted.

For the first three days approximately 100 grains of hexamethylenamin, well diluted, was given every twenty-four hours. On the day following the accident the temperature was 102° F. and the leucocytes numbered 20,800; two days later the leucocytes were 8,600 and thereafter remained within normal limits. The temperature slowly fell to normal and at no time was there any evidence of a meningeal infection. The lacerated wounds on the face healed rapidly, but there was a constant escape of cerebro-spinal fluid from both nostrils for twenty-five days. For twenty-eight days the average daily amount of hexamethylenamin was 70 grains a day; at no time, however, was there the slightest evidence of digestive disturbances or renal irritation.

Bursting Fracture of the Skull with Local Depression over Left Frontal Lobe; Simple Fracture of One of the Small Bones of the Hand; General Streptococcus Septicæmia; Cerebral Abscess; Meningitis; Recovery.

Surgical No. 26092. William P., age 7½. Admitted to the Johns Hopkins Hospital on June 13, 1910, with the following history: Three days previously was struck, from behind, by an automobile and thrown violently to the pavement. For an hour the patient was unconscious, and vomited once about four hours after the accident, but as there was no scalp wound other than a superficial abrasion over the left eye, and no bleeding from the nose or ears, the injury was not regarded as serious. The following day, however, the temperature suddenly rose to 103.4° F. On admission to the hospital, 48 hours after the injury, there was definite rigidity of the muscles of the neck, a positive Kernig's sign, a leucocytosis of 26,000, a low grade of choked disc and a temperature of 105° F. The cerebro-spinal fluid was cloudy and contained many pus cells; cultures showed the infecting organism to be a streptococcus.

On inquiring into the past history it was found that the child had had frequent attacks of tonsillitis and for several days preceding the accident had been feverish and complaining of a sore throat. On examination the whole throat was found to be inflamed, and there were small patches of exudate on the tonsils; a smear showed that the predominating organism here also was a streptococcus.

A decompressive opening was made under the temporal muscle on the left side but without disclosing any abnormality other than a tense œdematous brain. An incision into the bruised area over the left eye, however, unexpectedly disclosed a fracture from which pus exuded, and on further investigation a definite cavity was found in the left frontal lobe, from which there was an escape of infected, fragmented, cortical substance. Two days later the operative wound became infected and opened; a streptococcus abscess also developed around a fractured metacarpal in the right hand. Both infections were evidently hematogenous in origin, since there was no abrasion of the skin overlying the injury in the hand, and a streptococcus was recovered in cultures from the circulating blood.

Subsequent Therapy.—With the exception of the decompressive operation, and a lumbar puncture on three occasions for diagnostic purposes, an almost continuous administration of hexamethylenamin constituted the only treatment given in this case. From June 13 to July 4 (22 days) this child—7½ years of age—was given 939 grains of hexamethylenamin, a daily average of 42½ grains. During the first forty-eight hours after admission 291 grains were given, but insufficiently diluted with water, and on the following day the urine contained red blood cells and albumen. The additional administration of 100 grains on June 17 was followed by a marked hematuria, nausea and vomiting. The urine rapidly became normal, however, and the gastric symptoms entirely disappeared on withholding the drug for twenty-four hours and forcing liquids. Unfortunately, observations were not made to determine the concentration of the drug in the cerebro-spinal fluid or the circulating blood, or to follow by daily cultures its effect upon the organisms in either of these situations.

The following table illustrates the method which we employ in giving large doses of hexamethylenamin. Aside from personal idiosyncrasies, this drug will rarely cause irritative symptoms, if sufficiently diluted.

[11] It is scarcely necessary to state that there have been several cases of compound fracture of the skull in which death was due to hemorrhage or cerebral injury; such cases, however, are not included in the series mentioned above.

[12] It is of interest to note that there was no serious lesion of the kidneys in this case and that the hematuria was due entirely to an hemorrhagic cystitis.

Date.	Amount of hexamethylenamin given during 24 hours.	Method of administration.	Amount of liquids given during 24 hours.	Urine.	Highest temperature during day.
1910 June 13	135 grs.	By rectum.	250 cc. salt solution.	Normal.	105° F.
June 14	156 grs.	40 grains by rectum. 116 grains by mouth.	In 400 cc. salt solution. In 782 cc. (water, milk and broth).	Normal.	103.8° F.
June 15	90 grs.	60 grains by rectum. 30 grains by mouth.	In 300 cc. salt solution In 1050 cc. (water and nourishment).	Trace of albumen and a few red blood cells.	105° F.
June 16	.....	.....	500 cc. salt solution. 1290 cc. water and nourishment.	Trace of albumen and a few red blood cells.	104° F.
June 17	100 grs.	40 grains by rectum. 60 grains by rectum.	In 200 cc. salt solution. In 300 cc. salt solution.	Marked hematuria. Albumen and casts.	103° F.
June 18	.....	.....	1860 cc. by mouth.	Hematuria less marked.	102° F.
June 19	38 grs.	2 grains in every oz. of liquid by mouth.	1710 cc. by mouth.	Urine clear.	101.4° F.
June 20	81 grs.	2 grains in every oz. of liquid by mouth.	1800 cc. by mouth and by rectum.	Urine clear.	101° F.
June 21	68 grs.	1 grain in every oz. of liquid by mouth.	1650 cc. by mouth and by rectum,	Urine clear.	100.6° F.
June 22	41 grs.	1 grain in every oz. of liquid by mouth.	1410 cc. by rectum.	Urine clear.	100° F.

June 23d to July 4th from 15 to 30 grains of hexamethylenamin were given each day. The urine remained clear, and the patient was discharged apparently normal in every way; also was perfectly well when seen one year later.

Hypophysis Cases.

During the past three years there have been forty cases of hypophysis tumor, in the Johns Hopkins Hospital, in which the neighborhood symptoms were sufficiently marked to warrant an operative interference. The operation, as described by Dr. Cushing,[13] consists in the removal of the floor of the sella turcica, by an approach through the nose and sphenoid sinus, and incision of the dural covering of the gland, in order to relieve local pressure symptoms. In each case hexamethylenamin has been administered as a prophylactic measure; from 40 to 60 grains are given during the twenty-four hours preceding the operation, and even larger amounts for several days after the operation.

In thirty-one cases there were no post-operative complications whatever; in nine cases there was an escape of cerebrospinal fluid through the nose for several days following the operation, together with an elevation of temperature, headache, slight stiffness of the neck and other symptoms suggesting a meningeal infection. Three of these cases finally succumbed with meningitis; the other six cases, however, recovered. The post mortem examination of the fatal cases showed that the operation had been misdirected and the cranial cavity entered anterior to the chiasm, directly inoculating the cortex with organisms from the mouth and nose.

[13] Cushing: The Pituitary Body, J. B. Lippincott Co., 1912. (To appear shortly.)

Cerebro-Spinal Fistulæ.

The constant discharge of cerebro-spinal fluid into the nasal cavity, or middle ear, is not an infrequent complication of a cranial fracture, and usually leads to a fatal outcome from a secondary meningitis. Also, following certain operative procedures for the relief of increased intracranial pressure, the fluid may find its way out, even through the most carefully closed wound, and form a fistula, which is a great source of danger and is often extremely difficult to remedy. Such a condition necessitates a frequent renewal of dressings, and though every precaution may be taken, the cerebro-spinal space ultimately becomes infected with skin organisms.

In such conditions hexamethylenamin has proven of great value as a protection against meningeal infection. Our original observation on the excretion of this drug in the spinal fluid was made on a patient in whom a fistula had developed after an operation for a cerebellar tumor; and although at the time when the drug was first given there was an elevation of temperature, rigidity of the neck and many pus cells and bacteria of various kinds in the fluid escaping through the fistula, the patient began to improve and ultimately made a complete recovery. We have subsequently had six cases in which there was a similar condition, and all have escaped a fatal meningeal infection.

Since it is possible, in many cases of this character, to collect a specimen of the spinal fluid for chemical and bacteriological tests, one can accurately determine the size of the dose and the frequency with which the drug should be given in order to render this fluid an unsuitable culture media. It has been our custom to give the drug in small doses at intervals of thirty minutes or one hour, rather than the larger doses at four or six hour periods, as is usually recommended. In this way the drug is well diluted and toxic symptoms are less likely to be produced by large doses. When given at frequent intervals the drug is constantly present in the cerebro-spinal fluid, as may be shown by chemical tests, and the concentration at *all* times is sufficiently great to exert an inhibiting influence on the growth of the infecting organisms.

Infections of the Ear.

An infection of the middle ear is always attended with danger; a cerebral or cerebellar abscess, thrombosis of the lateral sinus, or an extension to the labyrinth, with a secondary meningitis, are not infrequent complications. When such complications do arise, the outcome is usually fatal, since it requires training of a very special nature in order to be able to recognize the condition during the early stages, and to carry out the surgical procedure indicated. It is, therefore, of the greatest importance that all infections of the middle ear be considered serious, and from the onset every precaution taken to discourage an extension of the infectious process.

Since Barton and others have shown that hexamethylenamin is excreted by the mucous membrane of the middle ear, and when given in large doses tends to discourage the local infection, the administration of this drug is doubly indicated in cases of otitis media. Although we have not had an extensive

series of such cases, we have, however, repeatedly seen a diminution in the amount and a change in the character of the discharge follow the administration of hexamethylenamin.

In two cases hexamethylenamin has apparently checked the progress of an acute labyrinthine infection: the following case is given as an example:

Surgical No. 27692. E. M., age 34, was admitted to the Johns Hopkins Hospital on April 24, 1911. For two weeks there had been a profuse, purulent discharge from the left ear, which had suddenly ceased thirty-six hours before admission. When admitted to the hospital, the patient was unable to sit erect or stand on account of dizziness. There was extreme tenderness over the left suboccipital region, but none over the mastoid itself; the temperature was 100.5° F., leucocytes 19,000; complained of diplopia; and there was a definite low grade of choked disc. Most striking was the constant rotary nystagmus to the left, which, however, could be stopped and reversed by irrigating the external auditory canal on the left with cold water. Bone and air conduction were both absent on the left side, but normal on the right. The drum on the left was hyperæmic and tense.

The patient was immediately given 60 grains of hexamethylenamin, and thereafter 100 grains each day until the subsidence of the acute symptoms. Although the drum was not punctured at this time, the relief was almost immediate. The headache, vertigo, nausea and vomiting had all ceased within two days after the drug was first administered, and the patient was discharged, apparently well, on May 4, 1911.

Dr. Cushing has recently seen in consultation a similar case, in which the headache, vertigo and symptoms of meningeal irritation rapidly disappeared, after giving large doses of hexamethylenamin.

Infections of the Nose.

It has also been shown that this drug is excreted by the mucous membrane of the accessory nasal sinuses, and its administration during the early stages of an ordinary "cold" will probably prove of value in preventing the chronic infections of these cavities.

Poliomyelitis.

The observations of Landsteiner and Popper,[14] and Flexner and Lewis[15] on the transmission of poliomyelitis to monkeys have demonstrated, among other things, that in the earliest stages of this disease there is leptomeningitis preceding the involvement of the central nervous system proper. This fact is of the greatest importance and at once suggests the possibility that hexamethylenamin might be of value in this disease. This supposition was confirmed, to a certain extent, in 1911, by the experimental studies of Flexner and Clark.[16] These authors ascertained that when the virus of poliomyelitis is injected intracerebrally in monkeys, in whom hexamethylenamin is already present in the spinal fluid, and the drug is then administered by mouth daily thereafter, that in many of the animals so treated, first, the incubation period of the disease is prolonged (from six to eight to twenty-four days), and, next, the onset of paralysis is entirely prevented.

These experimental observations are of the greatest significance since they indicate that protection may be afforded during the prevalence of an epidemic by the administration of hexamethylenamin, and furthermore, that the paralysis may be prevented by giving this drug during the earliest stages of the disease.

For the past two years the Massachusetts State Board of Health has recommended that hexamethylenamin be given, both as a therapeutic and as a prophylactic measure, during the prevalence of an epidemic; and numerous cases have been reported in which the recovery without paralysis was ascribed to the hexamethylenamin therapy. Skoog,[17] for example, in 1910, reports five cases in which the disease was recognized and hexamethylenamin treatment given during the prodromal stage; three recovered without paralysis; one developed paralysis, and another, "cared for under unfavorable circumstances," died.

Realizing, however, that a large number of cases must be studied in order to arrive at any definite conclusion concerning the value of hexamethylenamin in poliomyelitis, the writer, at the suggestion of Professor Goldmann and Professor Paul Erlich, visited Denmark and Sweden in the summer of 1911, at which time there was an extensive epidemic throughout entire Scandinavia. Through the kindness of Dr. Madsen, of Copenhagen, and Drs. Hellström and Arnold Josefson, of Stockholm, the writer was enabled to visit the larger of the infectious hospitals and institute hexamethylenamin treatment in all patients admitted during the preparalytic stage of the disease. The Health Department in Stockholm also consented to enforce the administration of hexamethylenamin, for a period of two weeks, to persons known to have been exposed to infection.

Dr. Arnold Josefson, of Stockholm, kindly undertook to personally examine the cases and supervise the treatment. As yet a sufficient number of observations have not been made to warrant any definite statements in regard to the value of this measure; Dr. Josefson,[18] however, in a brief report, in September, 1911, states, that of the first thirty cases, in which hexamethylenamin therapy was instituted, six were treated from the second day of the disease; one from the first day; and one from the third day. Each of these eight cases recovered without paralysis. He has also seen many cases in a more advanced stage of the disease, with facial or abducens palsy, in which the further progress of the disease was apparently checked by the administration of large doses of hexamethylenamin.

Since poliomyelitis is endemic in Norway and Sweden, it is hoped that we may soon be able to publish observations on an extensive series of cases.

Since the publication of our original reports in 1908-1909, others have made use of this measure for certain groups of cases.

[14] Landsteiner and Popper: Ztschr. f. Immunitätsforsch. u. exper. Therap., 1909, II, I Teil, 377-390.

[15] Flexner and Lewis: J. Am. M. Ass., 1909, LIII, 1639.

[16] Flexner and Clark: J. Am. M. Ass., 1911, LVI, 585.

[17] Skoog: J. Am. M. Ass., 1910, LV, 1804.

[18] Josefson: Allm. Svensk. Läkartidn., 1911, No. 41. Hygiea, 1911, LXXIII.

Barton,[19] in 1910, experimentally demonstrated that hexamethylenamin is excreted by the mucous membrane of the middle ear; and in seven cases of suppurative otitis media he found that the administration of this drug was promptly followed by a disappearance of the infecting organisms and a cessation of the discharge. In a recent analysis of 9590 cases of scarlet fever Holmgren[20] finds that there was a complicating otitis media in over 21 per cent, the majority of the cases occurring in children under five years of age. Barton, however refers to a long series of scarlet-fever cases in which hexamethylenamin was given as a prophylactic measure, and comments on the notable absence of middle ear infections in the cases so treated. At any rate, since it has been shown that hexamethylenamin is excreted into the middle ear, and in amounts which suffice to cause the rapid disappearance of the infecting organism, it would seem advisable that this drug be given, as a prophylactic measure, to every case in which a middle ear infection is a possible or threatened complication.

Barton, Brown,[21] and others, in 1910, called attention to the fact that hexamethylenamin is also eliminated by the mucous membrane of the para-nasal sinuses; and clinically these authors have found this drug of value in the treatment of acute and chronic sinus infections. Dr. Brown, himself, was suffering from a chronic suppuration of the right antrum of many years duration; within forty-eight hours after he began taking hexamethylenamin, however, there was a marked improvement in the local condition, and six days later the discharge had practically ceased.

Armstrong and Goodman,[22] in 1911, found that hexamethylenamin is eliminated by diseased bronchial or pulmonary tissue. In twelve cases in which hexamethylenamin was given, including pulmonary tuberculosis, pneumonia, bronchitis and asthma, the sputum in each instance was found to contain formaldehyde. Vanderhoof[23] has recently reported a series of cases of bronchitis in which the administration of hexamethylenamin has apparently been of decided therapeutic value.

There have been numerous publications during the past two years recommending that large doses of hexamethylenamin be employed in the treatment of ordinary colds, tonsillitis and other nose and throat infections. Our own experience has led us to believe that this drug is often of the greatest value in aborting an acute coryza, provided it be given in large doses and during the earliest stages of the infection.

Gradle,[24] in 1911, and more recently Ziegler, and others, have found that hexamethylenamin is excreted into the anterior chamber of the eye, and is of value in the treatment of various ophthalmic infections.

In regard to the use of hexamethylenamin in the prevention and treatment of meningeal infections, many interesting observations have been made by Stockmeyer,[25] Brem,[26] Ibrahim,[27] Rowell[28] and Hald.[l.c.]

Stockmeyer, in 1911, reported two cases of epidemic cerebro-spinal meningitis, which are of exceptional interest in this connection; the onset occurred practically simultaneously and in both cases the meningococcus could be demonstrated in smears and cultures.

Case No. I was given large doses of hexamethylenamin as soon as the character of the disease was recognized; in Case No. II, no hexamethylenamin was given, but otherwise the treatment was identical. When first seen both patients were unconscious, temperature 39.8° and 40.4° C., with Cheyne-Stokes respiration and a marked retraction of the neck. The case receiving hexamethylenamin immediately began to show improvement, while the second case steadily grew worse and succumbed on the fifth day. Owing to the appearance of a few red blood cells in the urine, the drug was discontinued, with an immediate return of coma, rigidity and irregular respiration. Large doses were again administered at two hour intervals, and again the patient immediately began to improve; on three occasions, subsequently, the drug was discontinued and each time the clinical condition would rapidly become worse. At the time of the report, six weeks after the onset of the disease, the patient had apparently made a complete recovery, with the exception of "a slight weakness of the feet."

We have had similar experiences with this drug in the treatment of experimentally produced meningitis in animals, and in two clinical cases with a meningeal infection; also it is well known that chronic infections of the bladder or kidneys may temporarily subside during the period of active therapy, but tend to reappear as soon as the hexamethylenamin is withdrawn.

The case described by Brem is of interest, since careful studies were made in order to determine the concentration of the drug in the cerebrospinal fluid, and its influence on the cell count and number of the infecting organisms. In this case, clearly one of meningococcus meningitis, hexamethylenamin was not given until the fourth day of the disease; it was then given in doses of 15 grains, and later increased to 20 grains, four times daily. Although there was no marked change in the clinical symptoms following the administration of this drug, the colorimetric tests indicated that formaldehyde was present in the cerebro-spinal fluid in a concentration of about 1 : 50,000. The cells in the spinal fluid were diminished from 18,000 to 3000 and later to 990 in each cmm.; and the meningococci, which were present in stained specimens and in cultures before, could not be demonstrated after the drug was given.

The comparatively long duration (23 days) of this acute meningeal infection, together with the decrease in pressure, diminution in cell count, and disappearance of the meningococci from the spinal fluid, all tend to confirm our previous contention that hexamethylenamin is excreted into the cerebrospinal fluid, and if given at frequent intervals will render this fluid an unsuitable media for the growth of microörganisms.

[19] Barton: J. Am. M. Ass., 1910, LIV, 1940; Boston M. and S. J., 1910, CLXII, 896.

[20] Holmgren: Hygiea, Stockholm, 1911, LXXIV, 257.

[21] Brown: J. Am. M. Ass., 1910, LIV, 1308.

[22] Armstrong and Goodman: J. Am. M. Ass., 1911, LVI, 1553.

[23] Vanderhoof: J. Am. M. Ass., 1912, LVIII, 331.

[24] Gradle: Ophth. Rec., 1911, March.

[25] Stockmeyer: Allg. Wien. med. Ztg., 1910, LV, Nos. 4-5.

[26] Brem: N. Y. Med. J., 1910, XCII, 816.

[27] Ibrahim: Med. Klinik, 1910, VI, 1893.

[28] Rowell: J. Am. M. Ass., 1909, LIII, 1641.

It may again be emphasized, however, that the chief value of hexamethylenamin lies in its use as a prophylactic measure.

Hald (*l. c.*), in 1911, made a series of careful quantitative estimations in order to determine the concentration of hexamethylenamin in the cerebro-spinal fluid and blood-serum. The concentration of the drug in the spinal fluid, removed by lumbar puncture from forty-five minutes to one hour after giving the usual dose (1 gram for adults; 0.5 gram for children) varied from 1:16,000 to 1:20,000. In the majority of the cases the concentration in the blood-serum, removed at the same time, was from two to four times greater than that in the cerebro-spinal fluid.

Fiaschi, in 1908, made the interesting observation that if hexamethylenamin is given by mouth formaldehyde may soon afterward be demonstrated in the fluid contents of hydatid cysts. In the cases observed by Fiaschi [29] the cysts were either in the liver or omentum. No mention is made of the effect of the drug on the parasite.

Chauffard,[30] in 1910, relates in detail a number of cases in which an acute cholecystitis occurred during the course of typhoid fever, and gives temperature charts and other data showing the prompt relief which followed the administration of hexamethylenamin.

Riddle,[31] in 1911, published the results of some studies made on fowls; he found that when hexamethylenamin is fed to laying hens, this drug passes through the follicular and vitelline membranes and is deposited in the egg, where it undergoes decomposition, liberating free formaldehyde. Moreover, he found that the eggs from fowls receiving hexamethylenamin contain a sufficient amount of formaldehyde to act as a preservative; such eggs remain fresh and palatable for a much longer period than do the control eggs from untreated hens. Sodium salicylate and sodium benzoate, when fed to hens, cannot be detected in the eggs.

Toxic Symptoms.

Although hexamethylenamin, or its modifications, has been in common use for the past fifteen years, there are but very few reports in which serious toxic symptoms are ascribed to this drug. In 1894, Nicolaier called attention to the fact that some individuals seem to be especially susceptible to hexamethylenamin, and even when administered in small amounts (5 to 7½ grains) painful micturition and hematuria may result. In the experimental production of hematuria, however, this author found it necessary to give as much as 230 grains a day, for several days, to a dog weighing twenty kilos; and even then, after the subsidence of the acute symptoms, microscopic examination of the kidneys failed to disclose any evidence of permanent damage. Nicolaier has also given patients, suffering with acute infections of the genito-urinary tract, as much as 150 grains at a single dose, without ill effect.

[29] Fiaschi: Austral. M. Gaz., 1908, XXVII, 394; (also personal communications).

[30] Chauffard: Semaine méd., Paris, 1911, XXXI, 109.

[31] Riddle: Science, U. S., 1911, XXXIV, 887-889.

Maguire,[32] experimenting upon himself, injected 100 cc. of a 1:2000 solution of formaldehyde intravenously, and one hour later the urine was found to contain albumen; 263 cc. of a 1:2000 solution produced hematuria with blood clots, which entirely disappeared, however, within twenty-four hours; a third injection of 63 cc. of a 1:1000 formaldehyde solution was followed by sharp abdominal pains, diarrhœa, hematuria, and catarrh of all the mucous membranes. Ewing, Park, and Payne got like results from the injection of formalin in rabbits.

More recently, Frothingham,[33] studying the effect of the subcutaneous administration of hexamethylenamin on guinea pigs, found that from 7½ to 75 grains can be injected under the skin in these small animals without producing any apparent organic lesion. In some instances there was a local reaction and necrosis at the site of the injection.

Of 486 cases of typhoid fever in the Massachusetts General Hospital, referred to by Easton,[34] nearly all received from 8 to 10 and some 15 grains of hexamethylenamin three times a day, for a period of two to three weeks; there were three cases of painful micturition and two of hematuria. The symptoms in each of these cases rapidly disappeared after withdrawing the drug, and left no evidence of permanent damage.

In our experience there have been but very few instances in which toxic symptoms have resulted from the administration of large doses of hexamethylenamin, although we have repeatedly given from 200 to 300 grains daily for four or five days; even in children, doses of 100 or 125 grains a day, have produced no irritative symptoms, provided it was possible to administer the drug sufficiently diluted with water. We have abandoned the custom of giving this drug in doses of 10 or 15 grains at stated intervals, since it is often difficult to induce the patient to take, at one time, the 250 or 300 cc. of water in which doses of this amount should always be dissolved. In case the patient is very ill, the drug is usually administered per rectum, from 50 to 100 grains being dissolved in a liter of salt solution and allowed to slowly flow into the bowel, a drop at a time. In no case has there been the slightest evidence of undue irritation of the intestinal mucosa, when the drug is thus given, and as a rule the salt solutions are well absorbed, even after one or two weeks of almost continuous administration by this method. If the patient is able to take nourishment by mouth, from 2 to 3 grains of hexamethylenamin are added to every ounce of liquid, since the drug is practically tasteless, and it is often possible, in this way, to give from 60 to 100 grains a day without the patient's knowledge and without producing gastric or renal irritation.

In 95 of our cases in which the average dose of hexamethylenamin was 75 grains a day for ten days, painful micturition and hematuria occurred in seven instances. Two of these cases were fatal meningeal infections of otitic origin; the patients were desperately ill when brought to the hospital, and the drug was given in unusually large amounts, with the hope of checking the progress of the infection. A third was a case of tuber-

[32] Maguire: Lancet, 1900, II, 1709-1714.

[33] Frothingham: Arch. Internat. Med., 1909, IV, 510-515.

[34] Easton: Boston M. and S. J., 1905, CLIII, 195.

culous meningitis in a child seven years of age. In each of these cases there was a well marked hematuria, but at the post mortem examination it was apparent that it had its origin from the mucous membrane of the bladder and was not due to an acute renal irritation. In the remaining four cases the urine rapidly became normal on the withdrawal of the drug.

Although there are undoubtedly certain individuals who have a personal idiosyncrasy for hexamethylenamin, and even a small dose may cause uncomfortable symptoms—such as a skin rash, catarrh of the mucous membranes, gastric or urinary irritation—this fact does not invalidate the use of the drug. Aside from personal idiosyncrasies our experience has been that untoward symptoms usually arise as a result of insufficient dilution, and such symptoms have invariably disappeared on withdrawing the drug and producing active diuresis by forcing liquids.

THE EFFECT OF JAUNDICE, PRODUCED BY LIGATION OF THE DUCTUS CHOLEDOCHUS, UPON THE PANCREATIC SECRETION.

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We know very little about the quantitative and qualitative changes in the pancreatic secretion due to organic or functional disturbances. Even experimental knowledge of the pancreas is so far from complete that any contribution to the subject seems worthy of being chronicled.

The object of our series of experiments was to determine the effect of jaundice, produced by ligating the *ductus choledochus,* upon the amount of pancreatic juice, its rate of flow and its ferment-content. The method employed was first making a pancreatic fistula and studying the secretion from this with the different types of food, meat, milk, and bread; then performing a second operation, the ligation of the gall-duct, and again, after studying the pancreatic secretion after the same kinds of foods, comparing the two and drawing certain conclusions as to the influence of jaundice so produced upon this secretion. As is well known, the pancreas has two or three ducts, and in the Pawlow method used by us, the lowest of these was the one ligated. As Pawlow and Bickel and their students have shown, this secretion may be produced by the sight or smell of food, and may be inhibited or entirely stopped by various reflex nervous influences such as excitement, anger, the sexual feeling, etc., although, mainly through the work of Bayliss and Starling, we know that chemical influences, acting as a secretin, play the most important rôle in calling forth this secretion. The pancreatic secretion, especially the trypsinogen, must be activated by the enterokinase of the intestinal mucous membrane; usually there is enough mucous membrane about the mouth of the pancreatic duct in the Pawlow operation to furnish this activating agent, and it is rarely necessary to add intestinal juice from another animal. Probably in this necessity for activation by the enterokinase lies the reason for the absence of the pancreatic auto-digestion *intra vitam.* It must not be forgotten that certain substances besides enterokinase can activate the pancreatic juice, notably the soluble calcium salts (Abderhalden), while other substances, such as pus, may produce a markedly inhibitory effect.

The quantitative study of the pancreatic secretion shows that it varies markedly with the different foods, carbohydrate food furnishing the most juice, fat the least, while as a rule the richness in ferment is in inverse proportion to the quantity of juice; most investigators have noted a close correspondence of the quantity of bile to that of pancreatic juice secreted, although, according to Pawlow, fat stands between carbohydrate and proteid in its bile-forming power. As to the bile secretion, although markedly increased by the taking of food and by bile-absorption in the intestines, it is nevertheless in part independent of the processes in the digestive tract; in other words, there are substances constantly circulating in the blood which can stimulate the metabolic activity of the liver-cells and possibly, though this must be to a comparatively slight extent, there is a secretion arising through nervous influences (Fleig); the flow of the bile from the gall-bladder into the intestine depends on various influences originating reflexly from the duodenal mucous membrane. The activating power of the bile upon the pancreatic juice, especially upon its lipase, and its aid in fat absorption, must not be forgotten. When considering the effects of icterus, we must think of (1) those due to lack of bile in the intestine manifesting themselves in digestive disturbances, (2) those due to the bile circulating in the blood, especially the action of the cholates upon the nervous tissues, and (3) the disturbances produced in the liver-cells by the action of the concentrated bile under increased pressure. In the sudden death of the dogs in both our experiments these factors must be taken into consideration, especially the toxic effect of the cholates, although in all probability the stormiest and most severe nervous symptoms are due more to the harm done to the vital processes in the liver-cells, than to the direct action of the absorbed bile-constituents upon the nervous tissues. Von Reuss showed that ligation of the gall-duct in dogs produced a diminution of glycogen in the liver, and in rabbits markedly lessened the glycosuria after the Claude Bernard sugar-puncture, while Glube (Med. Klinik., 1911, No. 43) from

thirteen experiments on two dogs concluded that after ligation of the gall-duct the curve of secretion of the pepsin was reversed, and not only was the percentage of pepsin in the juice diminished, but also the absolute amount.

Although, clinically, we recognize that jaundice produces marked disturbances in the intestinal as well as in the gastric digestion, the cases in which this can be studied quantitatively are extremely few in number, while even along experimental lines, comparatively little has been done. In man, conclusions regarding the effect of various conditions upon the pancreatic secretion must be made from the rare, post-operative pancreatic fistulas, from the examination of the urine and fæces for the pancreatic ferments, from pancreatic juice obtained from the stomach after administering olive oil or from the duodenum itself by especially devised instruments, from the examination of the stools for fat or undigested nuclei, or of the urine for sugar and for the Cammidge reaction. None of these, however, has furnished very definite results, and so we are obliged to place much reliance upon animal experiments; but we must not forget, in their interpretation, that it is unjustifiable to assume that the conditions are the same in man as in animals, although probably in many respects they are.

Our experiments, eighteen in number upon two dogs, were carried out as follows: The dogs were operated upon under ether anæsthesia, and with the most careful aseptic technique; the lowest pancreatic duct, with a small area of mucous membrane surrounding its mouth, was separated from the intestine, and sewed into a small opening made in the abdominal wall; the intestinal wound and the abdominal incision were closed. Healing was perfect in the case of the first dog, but there was a slight infection about the mouth of the duct in the second. Three or four days after the operation, the dogs were in condition to be studied. After 24 hours fasting, milk, meat or bread in measured amounts were given, and the resultant pancreatic secretion carefully collected and measured. In the mixed specimen of every two hours, the trypsin and the diastase were quantitatively estimated, the experiment lasting for six hours after the feeding. Generally, a day or more under normal mixed diet was allowed to intervene before the succeeding experiment was made.

In the case of the *first dog,* three preliminary experiments were made with 150 ccm. milk, three with 150 grams lean, fat-free beef, and two with 150 grams bread, while in the case of the *second dog,* three preliminary experiments were made with 500 ccm. milk, and two with 150 grams lean beef. From these experiments we could obtain average figures for quantity, trypsin and diastase after milk, meat and, in the case of the first dog, bread for six hours after feeding; these figures will be found in the tables at the end of the article, and are expressed graphically in the subjoined curves.

The dogs were then operated upon the second time—ether anæsthesia and the same careful technique, of course, being employed; a double ligation of the *ductus choledochus* was made and the duct cut between the two ligatures so as to insure a complete absence of bile from the intestines. Two days later the dogs were in excellent condition and had entirely recovered from the immediate effects of the operation; experiments were then carried on as before in regard to the pancreatic secretion, although it was impossible to get either dog to take bread. In subsequent experiments, we hope by the use of soft carbohydrate foods, in soup or purée form, which may be given through the stomach tube, to obtain figures also after carbohydrate feeding. In the case of the first dog the experiment was carried on as before the ligation of the gall-duct, that is, the food was given to the dog after fasting 24 hours, and a day of feeding with mixed diet intervened before the next experiment, but the second dog was fed immediately after the experiment with one pound of horse flesh, and the next experiment begun the following morning. In the case of the *first dog,* one experiment with 150 ccm. milk, one with 150 grams lean meat, and one with no food were carried out, no further experiments being possible, as after the removal of the bile from the intestine death occurred in 7 days, while with the *second dog,* one experiment was made with 500 ccm. milk, and one with 150 grams lean meat, death occurring four and one-half days after operation. In each case the dog recovered rapidly from the immediate effects of this second operation, remained quite well for five days in the case of the first dog, and three days in the case of the second, and from then on lost weight and strength with great rapidity. The *autopsy* of the *first dog* showed that both operations were perfect, there was no peritonitis, the liver was enlarged, all the organs were very yellow, and the gall-duct was much distended, while, histologically, some pus-cells and red blood corpuscles were seen in the larger pancreatic duct. In the *second dog* there was no peritonitis, the liver was only slightly enlarged, all the organs were bile-stained, and there was about 500 ccm. of fluid apparently almost pure bile, in the peritoneal cavity as the proximal ligature had slipped from the gall-duct. This may have accounted for the slight difference in the two cases, and the earlier death of the second dog, as here obviously there was a far greater opportunity for the rapid absorption of bile into the general circulation.

In our experiments the diastase was determined quantitatively by Wohlgemuth's method. Five cubic centimeters of a one per cent soluble starch solution were added to each of a row of test-tubes to which pancreatic juice in decreasing amounts had been added, 0.5 ccm. in the first tube, 0.25 ccm. in the second, 0.125 in the third, etc.; the tubes were kept in the water-bath at a temperature of 37.5°-39°C. for a half hour, and after being cooled and having been almost filled with water, were tested with a drop or two of decinormal iodine solution. The diastatic units are the number of cubic centimeters of a one per cent starch solution which should be entirely digested in one-half hour by 1 ccm. of pure pancreatic juice. The trypsin was determined by the casein method, 2 ccm. of a one per

cent casein solution being in each tube with decreasing amounts of pancreatic juice, the tubes being kept in the water-bath for one hour, and then tested with acetic alcohol (acetic acid 1 ccm., alcohol 45 ccm., distilled water to 100 ccm.). The trypsin units, in other words the tryptic strength of the juice, are the number of cubic centimeters of a one per cent casein solution which would be completely digested by 1 ccm. of pure juice in one hour.

A survey of the accompanying figures and diagrams will show the results of our experiments, which in the main follow the law that the less the amount of juice the greater its richness in ferment and vice versa. The differences in the figures in the experiments with the same amounts of the same food, *e. g.*, milk, can probably be explained partly at least on psychical grounds, appetite, surrounding sights and sounds, etc. In the main, however, the figures in the individual experiments with the same foods harmonize quite closely, and the average figures for quantity, trypsin and diastase, may be regarded as fairly typical of the effect of the various foods on the quantity of juice and its ferment-richness. We, of course, are speaking now of the results of the experiments *before* the performing of the second operation. The antitryptic action of the pus probably explains the fact that no trypsin could be demonstrated in the first two experiments with the second dog, as even the addition of pure intestinal juice (enterokinase) from another dog failed to bring about digestion of the casein; with the disappearance of the pus from about the mouth of the pancreatic duct, the tryptic action of the juice became manifest, but always to a less extent than in the case of the first dog.

When we study, however, the figures after the ligation of the gall-duct, in other words, try to determine the effect of rapidly developing jaundice due to the complete occlusion of the duct upon the pancreatic secretion, we note at once that this is very marked—more juice being secreted now after milk than after meat, while the richness of the juice in diastase and trypsin was also, broadly speaking, practically reversed. The diagrams show this especially well. The first dog was especially interesting in that up to an hour before death, even although fasting, there was a constant flow of pancreatic juice averaging 6.4 ccm. per hour with 1280 diastase units and 4096 trypsin units in each cubic centimeter; this may have been due to stimulation of the pancreas by the circulating bile-stuffs.

In both cases death was sudden, although for the preceding 24 to 48 hours there had been a rapid loss of weight and strength; this sudden death may be accounted for by the loss of such a great amount of alkali, by disturbances in fat metabolism, by the effects of the circulating bile-stuffs upon the body, especially of the cholates upon the nervous tissues, or by changes produced in the liver cells by the action of the concentrated bile under increased pressure, thus possibly allowing toxins from the intestinal canal to reach the general circulation. The extremely good condition of each dog after the first operation would seem to show that the bile and intestinal juice can act vicariously in the absence or marked diminution of the pancreatic secretion, and that it is only after the shutting off of the bile, in addition, that processes develop which lead to death in such a short time.

From this series of experiments we may, we believe, draw the following conclusions:

1. After the ligation of the gall-duct and the consequent production of a rapidly developing jaundice there is a marked reversal in the pancreatic juice both as regards amount and ferment-richness after the different types of foods: there is more juice with milk than with meat, and where before, the trypsin or the diastase showed a definite increase, now a decrease would be likely to be met with and vice versa.

2. The removal of the bile from the intestine after the previous withdrawal of the major portion of the pancreatic secretion produces in a very short time a rapid loss of weight and strength, ending in sudden death, and emphasizes anew the great importance of the bile as a partial substitute for the pancreatic secretion if the latter is absent or markedly diminished.

Detailed figures of all the experiments and graphic representations of certain of these figures follow.

Dog A.—Operation for Pancreatic Fistula (Pawlow), Oct. 25, 1911. Preliminary study of the pancreatic secretion.

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch Units.	Trypsin in Casein Units.
Experiment 1:					
Oct. 30.	Milk, 150 ccm.	1	1.8 ccm.	5120	128
		2	2.5 ccm.		
		3	3.8 ccm.	2560	512
		4	1.6 ccm.		
		5	4.2 ccm.	5120	1024
		6	2.0 ccm.		
		Total,	15.9 ccm.		
Experiment 2:					
Nov. 1.	Milk, 150 ccm.	1	1.4 ccm.	640	2048
		2	.9 ccm.		
		3	.7 ccm.	320	4096
		4	1.0 ccm.		
		5	1.9 ccm.	1280	4096
		6	1.9 ccm.		
		Total,	7.8 ccm.		
Experiment 3:					
Nov. 3.	Milk, 150 ccm.	1	.7 ccm.	1280	....
		2	1.2 ccm.		
		3	1.6 ccm.	1280	....
		4	3.2 ccm.		
		5	4.4 ccm.	1280	....
		6	7.8 ccm.		
		Total,	18.9 ccm.		
Experiment 4:					
Nov. 6.	Meat, 150 grams.	1	44.8 ccm.	1280	8192
		2	46.2 ccm.		
		3	48.2 ccm.	1280	1024
		4	25.8 ccm.		
		5	8.8 ccm.	1280	2048
		6	8.2 ccm.		
		Total,	182.0 ccm.		

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch. Units.	Trypsin in Casein Units.
Experiment 5:					
Nov. 8.	Meat, 150 grams.	1	23.5 ccm.	1280	....
		2	4.4 ccm.		
		3	8.2 ccm.	1280	....
		4	6.9 ccm.		
		5	2.9 ccm.	1280	....
		6	7.6 ccm.		
		Total,	53.5 ccm.		
Experiment 6:					
Nov. 10.	Meat, 150 grams.	1	7.0 ccm.	1280	256
		2	.8 ccm.		
		3	5.2 ccm.	640	512
		4	12.9 ccm.		
		5	4.8 ccm.	1280	1024
		6	20.1 ccm.		
		Total,	50.8 ccm.		
Experiment 7:					
Nov. 13.	Bread, 150 grams.	1	35.9 ccm.	1280	512
		2	28.0 ccm.		
		3	15.6 ccm.	1280	1024
		4	9.1 ccm.		
		5	7.3 ccm.	2560	2048
		6	8.4 ccm.		
		Total,	104.3 ccm.		
Experiment 8:					
Nov. 15.	Bread, 150 grams.	1	71.8 ccm.	1280	512
		2	45.0 ccm.		
		3	22.4 ccm.	1280	1024
		4	12.4 ccm.		
		5	8.2 ccm.	1280	2048
		6	6.4 ccm.		
		Total,	166.2 ccm.		
Average figures:					
	Milk, 150 ccm.	1	1.3 ccm.	2347	1088
		2	1.53 ccm.		
		3	2.03 ccm.	1387	2304
		4	1.93 ccm.		
		5	3.5 ccm.	2560	2560
		6	3.9 ccm.		
		Total,	14.19 ccm.		
	Meat, 150 grams.	1	25.1 ccm.	1280	4224
		2	17.0 ccm.		
		3	20.53 ccm.	1077	768
		4	15.2 ccm.		
		5	5.5 ccm.	1280	1536
		6	11.97 ccm.		
		Total,	95.3 ccm.		
	Bread, 150 grams.	1	53.85 ccm.	1280	512
		2	36.5 ccm.		
		3	19.0 ccm.	1280	1024
		4	10.25 ccm.		
		5	7.75 ccm.	1920	2048
		6	7.4 ccm.		
		Total,	134.75 ccm.		

Operation: Ligation of the gall-duct. Nov. 17, 1911.

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch. Units.	Trypsin in Casein Units.
Experiment 9:					
Nov. 20.	Milk, 150 grams.	1	10.4 ccm.	1280	512
		2	31.3 ccm.		
		3	7.6 ccm.	2560	2048
		4	6.6 ccm.		
		5	21.6 ccm.	1280	512
		6	8.8 ccm.		
		Total,	86.3 ccm.		
Experiment 10:					
Nov. 22.	Meat, 150 grams.	1	10.3 ccm.	1280	2048
		2	13.8 ccm.		
		3	10.8 ccm.	1280	2048
		4	10.6 ccm.		
		5	11.8 ccm.	1280	4096
		6	11.9 ccm.		
		Total,	69.2 ccm.		

Dog B.—Operation for Pancreatic Fistula (Pawlow), Nov. 28, 1911. Preliminary study of the pancreatic secretion.

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch Units.	Trypsin in Casein Units.
Experiment 1:					
Dec. 4.	Milk, 500 ccm.	1	3.4 ccm.	640	....
		2	3.8 ccm.		
		3	2.6 ccm.	640	....
		4	3.1 ccm		
		5	4.9 ccm.	640	....
		6	2.5 ccm.		
		Total,	20.3 ccm.		
Experiment 2:					
Dec. 6.	Milk, 500 ccm.	1	2.2 ccm.	640	....
		2	5.9 ccm.		
		3	6.8 ccm.	640	....
		4	7.9 ccm.		
		5	7.2 ccm.	640	....
		6	11.4 ccm.		
		Total,	41.4 ccm.		
Experiment 3:					
Dec. 8.	Meat, 150 grams.	1	4.2 ccm.	640	128
		2	11.4 ccm.		
		3	13.7 ccm.	640	32
		4	14.2 ccm.		
		5	13.3 ccm.	640	64
		6	12.7 ccm.		
		Total,	69.5 ccm.		
Experiment 4:					
Dec. 11.	Meat, 150 grams.	1	14.1 ccm.	640	128
		2	10.5 ccm.		
		3	10.5 ccm.	640	256
		4	7.3 ccm.		
		5	3.3 ccm.	640	256
		6	1.7 ccm.		
		Total,	47.4 ccm.		
Experiment 5:					
Dec. 13.	Milk, 500 ccm.	1	1.4 ccm.	1280	512
		2	8.1 ccm.		
		3	8.8 ccm.	1280	256
		4	9.2 ccm.		
		5	4.9 ccm.	1280	512
		6	4.3 ccm.		
		Total,	36.7 ccm.		
Average figures:					
	Milk, 500 ccm.	1	2.3 ccm.	853	512
		2	5.9 ccm.		
		3	6.1 ccm.	853	256
		4	6.7 ccm.		
		5	5.7 ccm.	853	512
		6	6.1 ccm.		
		Total,	32.8 ccm.		
	Meat, 150 grams.	1	8.2 ccm.	640	128
		2	11.0 ccm.		
		3	12.1 ccm.	640	144
		4	10.7 ccm.		
		5	8.3 ccm.	640	160
		6	7.2 ccm.		
		Total,	57.5 ccm.		

Operation: Ligation of the gall-duct. Dec. 14, 1911.

Day.	Food.	Hour.	Amount of Juice.	Diastase in Starch Units.	Trypsin in Casein Units.
Experiment 6:					
Dec. 15.	Milk, 500 ccm.	1	2.3 ccm.	1280	1024
		2	2.8 ccm.		
		3	2.6 ccm.	1280	2048
		4	2.6 ccm.		
		5	2.7 ccm.	1280	4096
		6	6.8 ccm.		
		Total,	19.8 ccm.		
Experiment 7:					
Dec. 16.	Meat, 150 grams.	1	.2 ccm.	1280	4096
		2	.2 ccm.		
		3	.2 ccm.	160	128
		4	.3 ccm.		
		5	.1 ccm.	160	128
		6	.0 ccm.		
		Total,	1.0 ccm.		

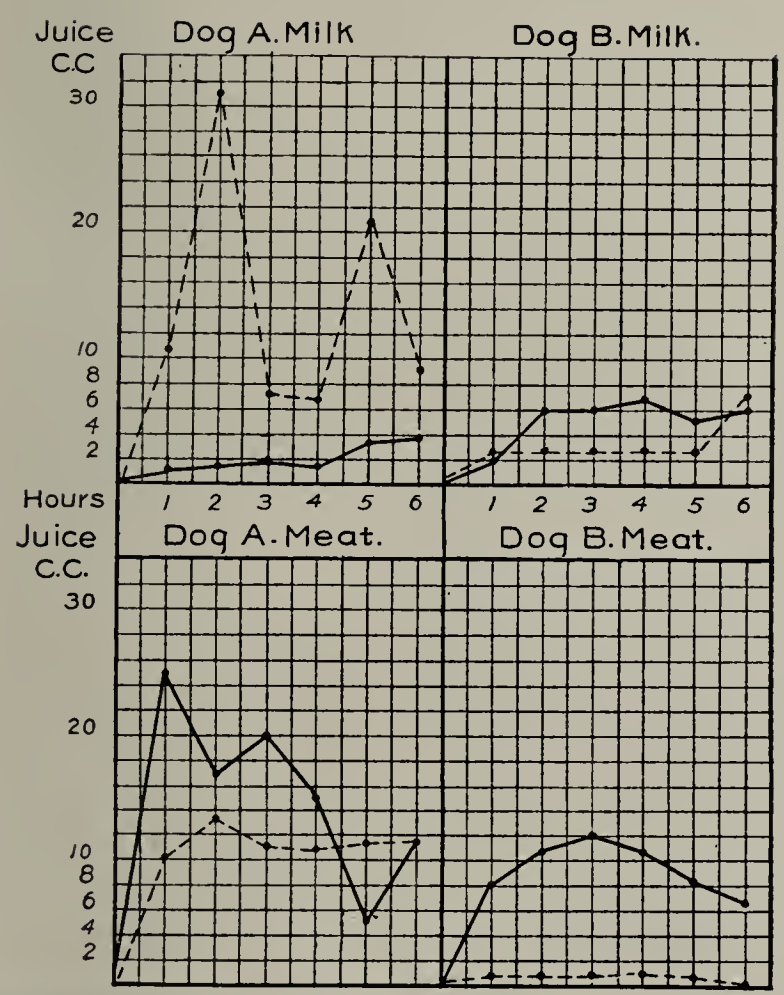
Studies on the Effect of Experimental Jaundice on the Pancreatic Secretion.

Average Curves.

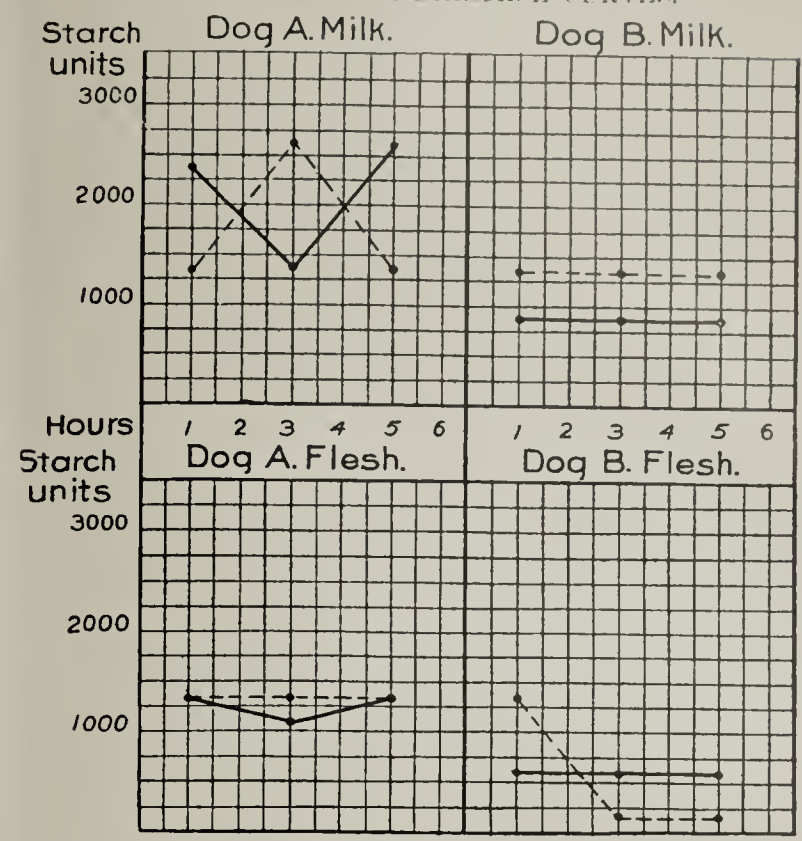
Quantity—curves with milk,
curves with meat.
Diastase—curves with milk,
curves with meat.
Trypsin—curves with milk,
curves with meat.

Before ligation of gall-duct ————
After ligation of gall-duct - - - - - -

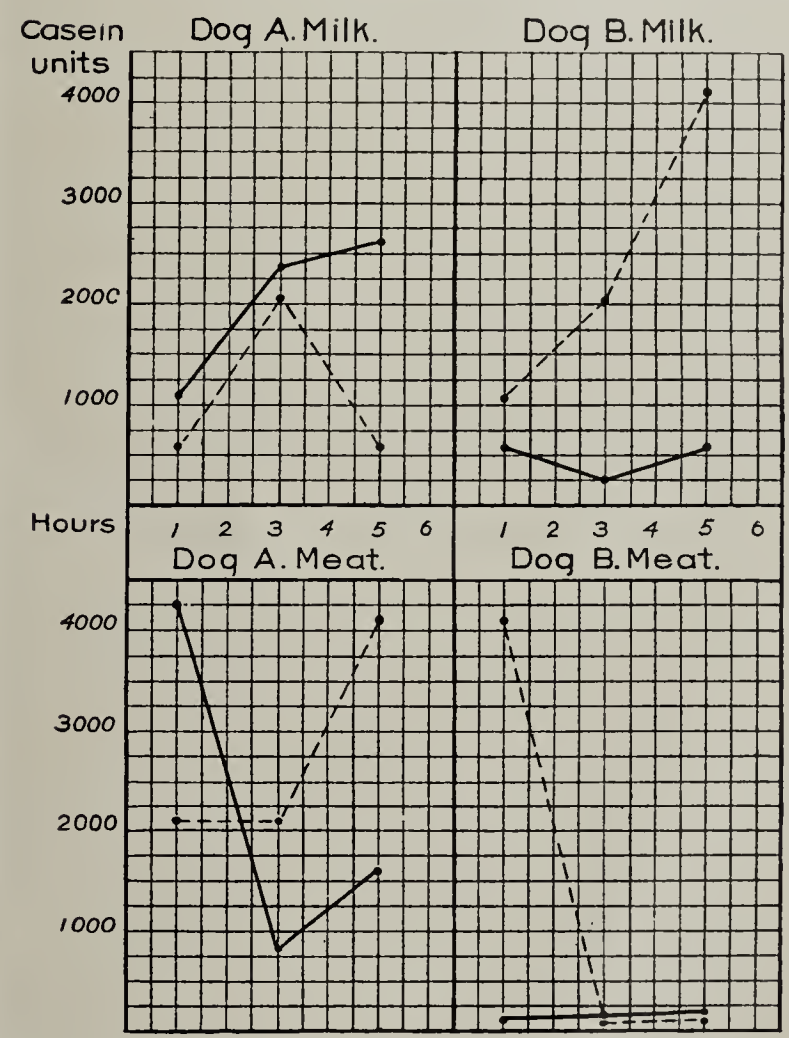
AVERAGE QUANTITY CURVES.



AVERAGE DIASTASE CURVES.



AVERAGE TRYPSIN CURVES.



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UNDESCENDED CŒCUM IN THE SUB-HEPATIC POSITION.

By Joseph Marshall Flint, M. D.

(*From the Continuous Surgical Service of the New Haven Hospital and the Surgical Laboratory of Yale University.*)

The importance of embryology in the interpretation of pathological conditions met at operations has frequently been emphasized. In fact, many pathological states have for their sole explanation the persistence of fœtal stages of development, where an arrest of the usual process of individual evolution has taken place. Many anomalies of the gastro-intestinal tract can be explained only on this basis as the following case shows. Although the embryonic condition maintained in this patient had no definite association with the disease which

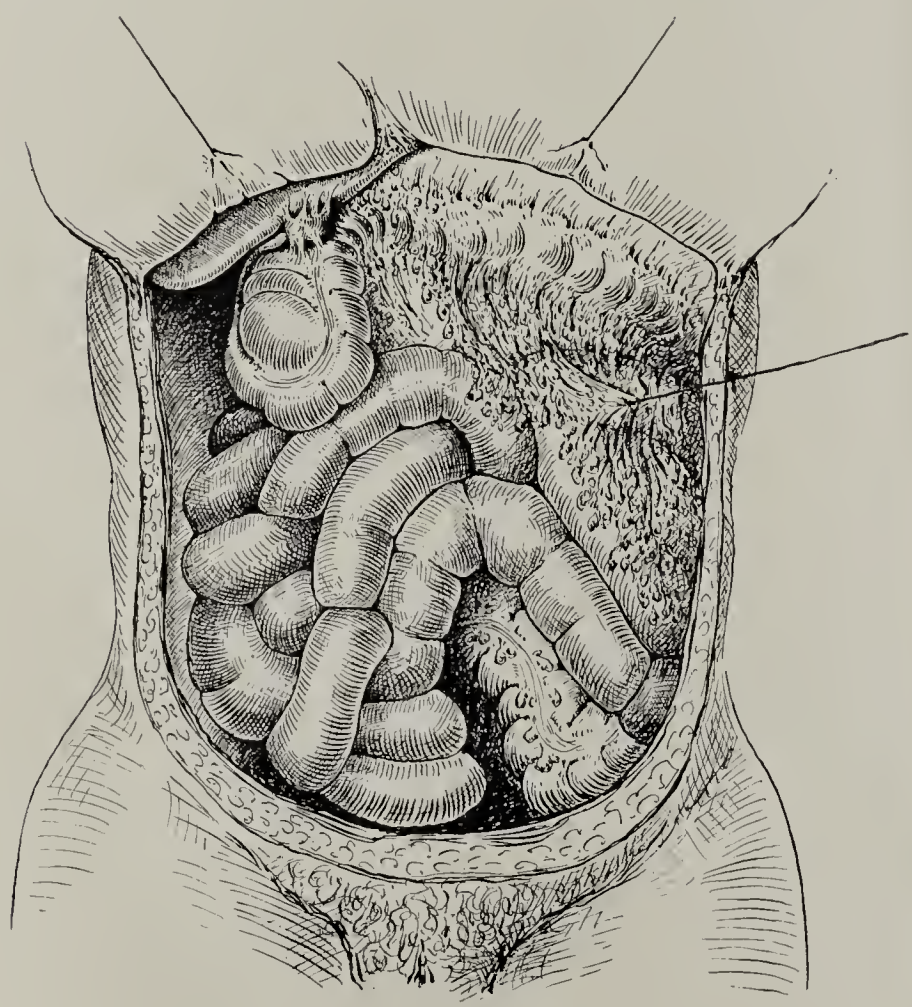

Fig. 1.

brought her to the operating table, it is nevertheless of great interest, for obviously a primary process beginning in the appendix would have led to great difficulties in diagnosis as in a case I saw some years ago in another clinic where an acute appendicitis gave a perfect clinical picture of an acute cholecystitis owing to adhesions between the tip of an abnormally long appendix and the fundus of the gall bladder.

The patient, Mrs. B., aged 38, has suffered for nine years from typical gall-stone colic with sharp attacks of pain at Robson's point which radiated to the costal margin and the right scapula. These attacks were of a sharp lancinating character and associated with vomiting, first of undigested food and then green slimy vomitus. The attacks have varied in frequency, but have averaged about every five or six months. Between attacks, she has suffered from indigestion chiefly in a feeling of fullness after eating and flatulence. She has never been jaundiced. Of late years, she has become accustomed to the pain and is never without a feeling of discomfort in the right hypochondrium. She has always been constipated, but recently the condition has become much worse. In other respects, she has been always quite well. Mrs. B. is the mother of five children and aside from the usual diseases of childhood, has had no other illnesses. She has never had typhoid fever.

The physical examination is in general negative except for a chronic parenchymatous nephritis. The liver is not enlarged. Over Robson's point there is distinct tenderness and muscle spasm on light palpation. Somewhat to the right, a small hard mass can be felt which is not sensitive to light pressure, but is painful on deep palpation. This mass is

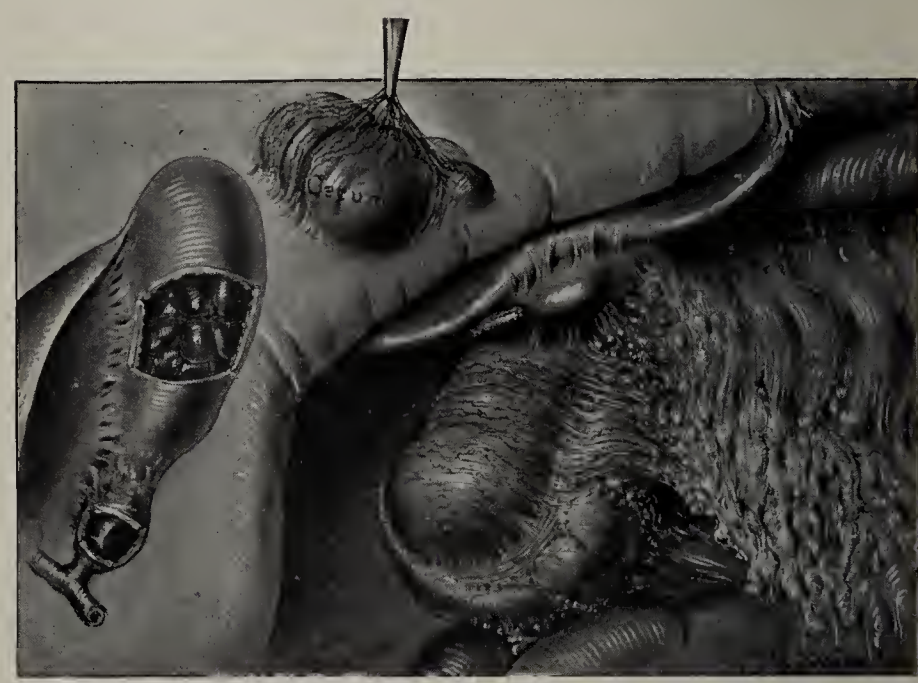

Fig. 2.

undoubtedly a thickened gall bladder. The remainder of the abdomen is negative.

The operation was carried out through a Kocher incision which revealed the conditions shown in Figs. 1 and 2. The cœcum lies just beneath the liver in the usual position of the hepatic flexure with an infantile type of appendix which lies under the cœcum and curls up so that its tip lies beside the fundus of the thickened and adherent gall bladder. Stretching over the cœcum is a thin veil which extends from its under surface and is continuous with the omentum. There was no ascending colon, the cœcum forming the right end of the transverse colon with which the omentum is fused in the usual manner. The gall bladder, much thickened and adherent to the cœcum, stomach, and duodenum, is filled with stones. A large stone lies impacted in the cystic duct. After separating the adhesions, a cholecystectomy was done in the usual manner. The appendix was also removed. The post-operative convalescence was uncomplicated. All drainage was removed on the thirteenth day and the patient discharged from the hospital on the twenty-fifth day with the wound entirely healed.

To understand the condition presented by this patient, it is necessary to recall the various stages in the development of the gastro-intestinal tract, from the simple straight tube with a ventral and dorsal mesentery extending as low as the level of the upper part of the duodenum and only a dorsal mesentery below that point. Where the increasing length of the lower segment carries it out into the umbilical cœlom, the primary rotation of the gut around the axis of the superior mesenteric artery occurs from the second to the third month, after which the intestine returns to the abdominal cavity. The rotation is completed within the abdomen and the cœcum takes the sub-hepatic position to the right side and just below the liver. Later, with the formation of the ascending colon, it descends into the right iliac fossa about the eighth month of fœtal life establishing conditions approximating those found in adult life.

At any of these fœtal stages, the process of development may be arrested or retarded yielding anomalous topographical relationships of the intestine. Instances have been recorded of failure of the intestine to rotate with a left-sided cœcum or the process may stop after rotation with the cœcum lying beneath the liver as in the instance recorded in this paper. On the other hand, the descent may be excessive and the cœcum become a pelvic organ.

Smith * has published an admirable review of the anatomical position of the cœcum based on observations made from a series of 1050 autopsies upon infants most of whom were under three months of age. From his paper, I quote the following table:

Position of Cœcum.	No. of cases.
Cœcum on left side without rotation of the intestine	5
Cœcum undescended in sub-hepatic position	63
Cœcum in right iliac fossa	882
Cœcum in pelvis	100
Total	1050

It will be seen that in the majority of cases, the cœcum is in the iliac fossa in what is considered its normal position. In 5 cases there was no rotation of the intestine, in 63 the condition presented by our case obtained, while in 100 the cœcum was found in the pelvis. There is, of course, an enormous difference between infantile and adult anatomy, making a large readjustment of the viscera necessary between the periods of infancy and maturity. Accordingly it is probable that many of these arrested, or, to describe them more accurately, delayed processes, are corrected before growth is completed as is shown so frequently in the late descent of an abdominal or inguinal testis. While the conditions shown in this table would not represent a fair average of 1000 similar autopsies on adults, it is of importance, however, to remember the possibilities of delayed or arrested development in the position of the viscera and the intestine.

It is apparent then that the condition presented by our patient is to be found in a state of arrested development of the intestine following the rotation of the gut leaving the cœcum in the sub-hepatic position. This usual descent of the cœcum with the formation of the ascending colon which occurs about the eighth month of intrauterine life failed to succeed the rotation and the cœcum was left, in consequence, in its fœtal position beneath the liver just adjacent to the gall bladder. In this instance, no ascending colon was present, so the cœcum formed simply a cul de sac on the hepatic end of the transverse colon occupying a position about the usual site of the hepatic flexure. Spreading over the cœcum was a typical membrane such as has been described by Jackson and variously termed Jackson's veil or membranous pericolitis. This membrane was continuous with the omentum and gradually and insensibly passed on from a typical veil into typical omentum as is shown in the illustration indicating the conditions found at operation. The importance of this feature of the case as affording a possible explanation of the origin of certain of these pericolic membranes, I shall discuss in a later paper. It is not impossible, however, that these membranes which are derived from the omentum or the secondary peritoneal fusions after the rotation of the intestine may be responsible for the failure of the cœcum to descend by fixing it permanently in the sub-hepatic position. For the moment I simply wish to emphasize this point and the interest of persistent embryological conditions in the pathology of the gastro-intestinal tract especially owing to the possible difficulties in diagnosis to which such misplacement may lead.

* Smith. Anatomical Record. Vol. 5. 1911.

THE PRESENT STATUS OF THE ANTI-TYPHOID CAMPAIGN IN GERMANY.*

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In that portion of the Rhine country where the Franco-German war was fought, now entirely controlled by Germany, before 1870 back to the days of Napoleon largely in the possession of the French, and previous to the Napoleonic campaigns the battleground of many a conflict between Teuton and Gaul, a fight has been waged against typhoid fever during the past decade which, to the well-trained medical man, is more full of interesting details than any of the collisions between the rival nations. To understand the motives which underlie this campaign we must consider for a moment the historical development of hygiene in Germany and picture to ourselves the con-

* Address delivered at the graduation exercises of the Naval Medical School, Washington, and before the Johns Hopkins Hospital Medical Society.

ditions in Alsace-Lorraine which led Robert Koch, in 1902, to inaugurate a new method of preventing the spread of typhoid fever.

Following the advice of the founder of modern hygiene, Max v. Pettenkofer, Professor of Hygiene in the University of Munich, and indeed the first professor of this subject in any German university, about the year 1870 the cities of central Europe began to adopt the measures which the wise Pettenkofer had advocated to control the diseases of the soil (the *Bodenkrankheiten*), Asiatic cholera, typhoid fever and dysentery. The city of Vienna, for instance, built within narrow walls, deriving its water supply from surface wells sunk in a sewage-permeated soil, had typhoid fever year in and year out. In the year 1874 a new supply of clean pure water was obtained from outside the city limits and within a year the typhoid mortality was cut in two, falling from 15-16 per cent to 7-8 per cent. The typhoid-infested Munich canalised its sewage system, washed these canals out with a branch of the river Isar, established a good supply of drinking water and eliminated the typhoid fever from its midst. Similar measures were equally effective in the other great cities of Germany, Berlin, Leipzig, Dresden and Frankfurt, freeing their population of this widespread scourge.

With the advent of the science of bacteriology and especially with the discovery of the cholera vibrio in 1883 by Robert Koch, the Munich school of hygiene founded by Pettenkofer lost ground. Their doctrines were no longer regarded as of such prime importance. Why indeed study the conditions under which the hypothetical etiological agent of a disease might multiply in the external world when the real living organisms which caused this disease could be studied in the laboratory? In consequence of this change of sentiment attention was more and more devoted to the sick patient and the paths by which the infectious agents were eliminated from his person. Especial impetus was lent this effort by the results obtained from the further study of the cholera vibrio. The perfection of a method by means of which the spirillum of Koch could be cultivated from the dejecta within 18 to 24 hours was indeed a wonderful boon to the new sanitarians. The recognition of Asiatic cholera in its early stages and the quarantine of a country against infected individuals constituted a far simpler procedure for controlling this disease than was furnished by the elaborate measures of Pettenkofer and his pupils.

The cultivation of the typhoid bacillus by Gaffky in 1884 was hailed with almost as much enthusiasm as greeted the discovery of the cholera vibrio by Koch. The etiology of another disease was settled. The control of another pestilence was brought to medicine by the bacteriologist. Nothing is more striking in the history of bacteriology than the bitter disappointment which followed Gaffky's achievement. The typhoid bacillus proved hard to differentiate from the other microörganisms of the intestinal tract. It had no characteristic morphology which would call attention to its presence in suspected individuals. Its cultural properties were somewhat difficult to work out and only the most skillful bacteriologists could identify it with any degree of certainty. Finally the organism could not be found in such vehicles as water and milk even though fairly complete epidemiological evidence could be presented to show that the disease was spread through their agency. Despite constant efforts to solve the problem, the life history of the typhoid bacillus outside the human body remained shrouded in mystery. The hygienists of the old world were thus forced back to adopt the preventive measures against typhoid fever originally advocated by Pettenkofer, even though the infectious agent of the disease was now in their grasp. The measures suggested by the Munich school continued to be employed. Pure water was brought to the great centers of population from remote and unoccupied areas, or the water at hand was purified by filtration, the garbage of the cities was destroyed by incineration and the sewage so treated that its noxious properties were eliminated.

In consequence of these sweeping reforms in municipal hygiene, typhoid fever, which had previously been one of the most widespread diseases in Germany became one of the rarer. The experience of the city of Hamburg may be cited to indicate how effective the work of the sanitarians had become in controlling this disease. The great cholera epidemic in this city in 1892 had emphasized the rôle of impure water in the spread of Asiatic cholera and extensive filtration plants were established to purify the water of the river Elbe. Other hygienic changes were instituted at the same time in this ancient commonwealth under the direction of Professor Dunbar, a pupil of Gaffky. As a result of the measures adopted, not only did cholera die out of Hamburg, but typhoid fever as well. So effective indeed was the work of sanitarians throughout Germany that the water-borne diseases diminished steadily in frequency from year to year. In Prussia, for instance, where the typhoid mortality had at one time been so high as to have a definite influence on the total mortality, it fell from 2.4 deaths per 10,000 living, in 1889, to 1.33 in 1899 and 0.81 in 1902 (Kirchner (1)).

Typhoid fever, nevertheless, was by no means under control in Germany. It still continued to appear in the smaller towns and villages and in the country districts. Occasionally great epidemics broke out, as in Berlin in 1887-1888, where the disease was traced to an infected water supply and in Westphalia in 1900-1901, where 3000 cases and 350 deaths were attributed to the same cause. The more accurate study of the disease, moreover, indicated that other agencies than water might be operative in carrying the infection from person to person. The importance of milk especially, as a means of transmission, was brought out in Hamburg, as in Sweden, where the public dairies were found responsible for many cases of the disease.

The obscure points in the epidemiology of typhoid fever had long been recognized by Robert Koch, who was clearly aware of the difficulties connected with the isolation of the typhoid bacillus from the stools, and its early identification in the laboratory. To no one more than to the discoverer of the cholera vibrio was the necessity apparent of finding means of establishing a rapid diagnosis of typhoid fever by methods

similar to those which were employed for Asiatic cholera. At Koch's suggestion, and under his personal direction, the members of the staff of the *Institut für Infectionskrankheiten* in Berlin undertook a thorough systematic study of Gaffky's bacillus in all its phases. So many improvements in technique were soon introduced in the Berlin Institute, and also in a number of other bacteriological laboratories, that by the year 1902 Koch thought the time was ripe for inaugurating a new movement. Among the most important advances in knowledge which placed the diagnosis of the disease and the recognition of the typhoid bacillus upon a firm basis, should be mentioned the discovery of the agglutinins by von Gruber and Durham, the special media of v. Drigalski and Conradi, and the technical methods devised by Endo, Ficker and Lentz. (The importance of the fermentation tube introduced by Theobald Smith for the study of the typhoid-colon group of organisms has apparently never been recognized in Germany.) On November 28 Koch (2) proposed at the meeting of the Scientific Senate of the *Kaiser-wilhelms Akademie* that the campaign against typhoid fever should be taken up from a different standpoint. He called attention to the old Prussian law of 1835, 8, VIII, which provided that certain measures should be adopted to control the spread of a prevalent disease of the times. The disease, as we now know, was a conglomerate, including cases of spotted fever (*Flecktyphus*), recurrent fever (*Rückfallfieber*) and typhoid fever (*Unterleibtyphus* or *Abdominaltyphus*). To ward off an attack of the disease the measures provided for the avoidance of crowded rooms, pure air, cleanliness and dietetic regulations. To prevent its spread the sick should be separated from the well by isolation, their houses should be placarded, and, after recovery, the effects and the dwellings of the patients should be disinfected. The framers of the law evidently believed that the disease was communicable from person to person. Koch also called attention to the widespread doctrine deeply engrained in the minds of the medical public that typhoid fever was chiefly water-borne, despite the early recognition of its contagiousness and despite the clear evidence that the infectious material could be conveyed directly from individual to individual, as from the sick patient to the doctor, the nurse, or the orderly. Koch further emphasized the continued occurrence of the disease in the country districts, especially in the Rhine provinces and in some of the cities like Metz, Strassburg, and Saarbrücken, which had been the scenes of important battles between the Germans and the French. It seemed indeed as if a large part of the typhoid fever still found in Germany was the heritage from the war with France, remaining uncontrolled in those districts which had a French population or which had been occupied for some periods of time by French troops.

The danger to German military power arising from these constant epidemics of typhoid fever in Alsace-Lorraine was clearly recognized by the authorities. As Bismarck the Iron Chancellor had said, the Rhine provinces would always be the seat of conflict between France and Germany, the threshold of wars between the rival countries. They should, therefore, be under the power and control of Germany. Little advantage could be expected from this German control, however, unless the infectious diseases there could be regulated, especially such pestilences as typhoid fever.

Following Koch's suggestion, a trial typhoid station was established at Trier, the district which more than all others in Prussia had persistently had a high mortality from typhoid fever. The work here was undertaken by Prof. Frosch, Dr. v. Drigalski and Dr. Conradi and various prophylactic measures were tried out by these investigators to determine whether they were capable of application on a more extensive basis. When the work began at Trier, seven cases of enteric fever had been reported to the authorities. By careful examination of the population of this community and especially by a painstaking study of a large number of individuals suffering from obscure symptoms of illness, their blood being tested for agglutinins, their urine and stools being examined for the typhoid bacillus, it was soon brought to light that there were in reality not seven but sixty-four cases of typhoid of whom 70 per cent were in children. These cases were carefully isolated, their effects and dwellings disinfected. In three months the investigators believed that the four villages in the district of Trier, Waldweiler, Schildingen, Heddert, and Mandern were free from typhoid fever. No hope was entertained, of course, that this freedom would persist. A number of important advances in our knowledge of this infection were brought out by this work in Trier. Not only was it established that many mild attacks of fever without the classical typhoid symptoms were in reality genuine cases of the disease, but it was clearly shown that, contrary to general belief, children were particularly susceptible to infection. This was a point of considerable epidemiological importance, since the range of activity of children, especially of boys between the ages of eight and fifteen, is far greater than that of adults. Imagine the number of different localities the average boy will visit and the number of different individuals he will come in contact with on a long summer day, in a little village community. Possibly, however, the contribution of the greatest importance which came from this first typhoid station was the conception of the "bacillus carrier." From the observations of Frosch, v. Drigalski, and Conradi in Trier on typhoid fever, it was shown that the typhoid bacillus is present in the dejecta in two groups of individuals. One group includes those persons who have recovered from characteristic attacks of the disease and who continue to harbor and excrete the organism for long periods of time, the chronic excreters or *Dauerausscheidern.* The second group includes those individuals who have been infected with the typhoid bacillus, who have no symptoms of the disease or symptoms so mild as not to present themselves and yet give off the typhoid bacillus for indefinite periods, the chronic carriers, *eigentliche Bacillenträger.*

With the station at Trier as a model, others were established at points where typhoid was especially prevalent, as at Saarbrücken, where the second was located. July, 1903, may be said to mark the beginning of the systematic campaign against typhoid fever in southwest Germany. Eleven stations were instituted, four principal ones at Saarbrücken in Trier, at Landau in the Bavarian Rheinpfalz, at Metz in Lothringen,

and at Strassburg in Unterelsass, and seven accessory ones at Saarlouis, Neunkirchen, and Idar in Trier, at Kaiserslautern in the Rheinpfalz, at Diedenhofen in Lothringen and at Hagenau in Unterelsass. How closely these stations corresponded in location to important points of the Franco-German war is evident from the establishment of principal stations at Metz, Strassburg, and at Saarbrücken, the three communities which possibly as much as any others were the site of stubbornly fought campaigns in this great conflict.

By the end of the year 1904 these eleven institutes were established upon an orderly and lasting basis, *Herr Geheim Regierungsrat* Schneider of Hannover being selected to control and regulate the entire organization. Since then the work has gone steadily on, the men selected to direct the various laboratories showing an enthusiasm for their work, and an appreciation of its significance, both hygienic and political, which is almost without parallel. While three of the institutes originally established have been abandoned, the powers and privileges of the others have been amplified. The example of Prussia has not only had a beneficial effect upon her immediate neighbors, three stations being established by the Bavarian Government shortly after the movement was inaugurated by Prussia, but an enormous interest in the study of intestinal infections has been stimulated over the entire civilised world.

As a result of this systematic campaign against typhoid fever our knowledge of the disease has been increased during the past ten years, one might say, almost ten-fold, and one need but glance over the pages of the *Klinisches Jahrbuch* to realise the great extent of this work and the importance of the many publications which have come from these various laboratories. Indeed our entire conception of enteric fever has undergone a great change, and while we still recognize the fact that water, milk, and food may serve as the means of transmitting the infectious material from person to person, we are more and more convinced that in certain communities at least the majority of cases are due to contact either with a case of the disease or with a bacillus carrier. How easily the living organisms may be carried from sick to well is shown by such observations as those of Seige (3), who describes a house in Alsace-Lorraine, where he found a typhoid patient lying on a bed covered with a rubber mattress. The urine and the dejecta of the patient had been spilled upon this mattress, had then fallen to the floor and there been allowed to dry. In the same house Seige found a flask of disinfectant left by the medical attendant, with its cork still intact. Or the observations of Frosch (4) may be cited, who saw a woman empty the vessels containing the urine and feces of her typhoid-stricken husband in the intervals of preparing the evening meal for the other members of her family. How simply a bacillus carrier can give rise to a milk epidemic of the disease is quoted by the same author, who noticed a maid who had just recovered from a characteristic attack and who was known to harbor and excrete the organisms going directly from the water-closet to the dairy where, without even washing her hands, she began her daily task of milking. Furthermore, the extent to which the typhoid bacillus is given off by patients and convalescents has been found to be far greater than previously supposed. Frosch (l. c.) has pointed out that the bacillus is found in 80 per cent of all cases for a period of three to four weeks after the termination of the fever and Lentz (5) has shown that the excretion of the organism, if it does not cease within ten weeks, lasts almost indefinitely. In such cases this species seems to replace the normal bacteria of the intestinal tract, appearing in the dejecta in large quantity, sometimes in almost pure culture. If the organisms persist primarily in the gall bladder, from which point they find their way into the intestines, they must indeed find in the bowel itself favorable conditions for an enormous multiplication. Their presence in the dejecta of certain individuals is far too great to permit us to believe that they are harbored in the gall bladder alone. The organisms, moreover, are fully virulent, agglutinate with an anti-typhoid serum, and give the Pfeiffer phenomenon. So far as laboratory tests go, they have the same characteristics as those isolated from an acute case of enteric fever. Finally, as Prigge (6) has indicated, by far the greater proportion of the chronic carriers are women. Thus far no drugs have been found which have any lasting influence upon the number of typhoid bacilli given off by these individuals or the length of time they may continue to harbor and excrete the organisms.

While the literature describing the methods of this campaign in Germany is ample and the many important results obtained have been published with great care, a full appreciation of the inner working of a typhoid station is manifestly difficult to obtain from reading alone. The personal factor, the spirit and enthusiasm which the director of a laboratory inspires in the group of workers gathered about him, seldom if ever appear in the pages of a printed report. Feeling the inadequacy of my knowledge of the subject and desiring to acquaint myself with the more intimate details of this great work, I took occasion last September to go to Saarbrücken, where one of the principal stations already referred to is located. Through the kindness of the Director of the Institute, Dr. Prigge and his assistant, Dr. Rommeler, I was permitted to spend several days in the laboratory and was shown the practical organisation of an anti-typhoid station.

Saarbrücken is situated a little over a hundred miles from Strassburg and was the scene of many stirring events in the war of 1870. It has at the present time about 100,000 inhabitants and is the center of important mining and manufacturing industries. The people in the city itself and in the surrounding country districts are a curious mixture of races. The original inhabitants seem to be of French origin. While not speaking French, the language still prevalent in a large part of Alsace-Lorraine, the peasants, to the casual observer at least, resemble the French much more than the Germans in general physiognomy and characteristics. Added to this indigenous population is a large element of Prussians, principally workmen who have moved there in considerable numbers to take the situations offered in the mines and factories. Finally a corps of the German army is quartered in the city of Saarbrücken, adding a new and important strain to this heterogeneous population. From this country typhoid fever has never disappeared.

Epidemic after epidemic has visited the city of Saarbrücken, summer and winter alike, and the disease has remained endemic in small foci in the rural districts. So high indeed has been the death rate here that the first principal station to be established by the Prussian Government was located at this point.

The laboratory building in Saarbrücken, where the work of the station has been carried on now for eight years, was originally a small boy's school. It contains but one large workroom fitted up with the apparatus usual in a bacteriological laboratory, a preparation room for the manufacture of media and a small office for the administrative end of the work. Provision is made for a certain amount of experimental investigation on animals in the adjoining courtyard. What a lesson for those of us who are disposed to estimate the magnitude of scientific work by the size of the buildings in which the work is done. To this station is reported every case of typhoid fever or every case of illness with typhoidal symptoms occurring in Saarbrücken and in the adjoining country for a distance of about ten miles. The population represented in these two areas is nearly 200,000. Specimens of blood from all suspected cases are sent to the station where they are tested for typhoid agglutinins and also for para-typhoid and dysentery agglutinins. In addition, the stools and urine from such cases are also sent if the diagnosis remains in doubt. For all cultures the v. Drigalski-Conradi medium is employed in large Petri plates measuring 7-8 inches in diameter. All blue colonies which develop on these plates are immediately tested with a powerful anti-typhoid serum, an anti-para-typhoid and an anti-dysentery serum. Should agglutination of the organisms occur with any of these sera, the organisms are cultivated and identified. As soon as a diagnosis of typhoid fever is established in any case the patient is removed to the hospital in Saarbrücken. This removal is practically compulsory. The sanitary regulations provide that all cases must be sent there unless adequate arrangements can be made elsewhere for their isolation and proper care. Since the population of the district, especially outside the city limits, is extremely poor, it is very exceptional for a typhoid patient to be kept at home. While in the hospital the cases are entirely under the control of the hospital authorities, the blood, urine, and stools being examined in the laboratory there and not at the station. A convalescent can only be discharged after two consecutive examinations have failed to reveal the typhoid bacillus in his dejecta. If, however, the organisms persist beyond a period of ten weeks, then the individual can no longer be legally or forcibly prevented from leaving the institution. He may go when and where he chooses. In such cases the sanitary acts provide only that the infected person must be informed of the danger he exerts towards the people with whom he comes in contact and that he must be instructed in the methods to be employed for the disinfection of his excreta. To determine the length of time these remain infectious he must send samples or urine and stool to the laboratory for examination or permit members of the laboratory force to collect such samples from his premises. This provision gives the station its control of the population of the district. Every bacillus carrier is known and watched. Large charts in the institute show the location of every house where typhoid fever has occurred during the past eight years and the dwelling of every known carrier. Whenever a new case of the disease occurs, or a small epidemic breaks out, the association of the new cases with the old can be worked out, sometimes with apparent ease.

Following the removal of any typhoid patient to the hospital, the district physician (*Kreisarzt*), in company with some member of the staff of the institute, visits the premises of the infected person. A careful survey of all the sanitary arrangements of the place is undertaken, especially those concerned with the disposal of excreta and garbage. The water, milk, and food supplies are thoroughly looked into. The members of the family are questioned as to the possible source of infection. Finally all the other inmates of the dwelling are overhauled, to determine the existence of any mild or concealed cases of enteric. On the appearance of the slightest symptoms suggestive of a typhoid infection, specimens of blood, and frequently of urine and stools are sent to the laboratory for study. In this way nearly all the cases of typhoid fever which may occur among the patient's associates in the district of Saarbrücken are eventually brought to light.

I had the pleasure of accompanying Dr. Engels, the district physician and Dr. Rommeler of the institute, on several trips, and I could not but be impressed by the thoroughness with which the inspection was made and the wisdom of the measures suggested, always touching the essentials of cleanliness and yet always, as far as possible, within the means of the families visited. Most interesting was the harmony which apparently existed between the populace and the representatives of the authorities. On the one side the poor people showed themselves thoroughly amenable to instruction and advice from the physicians, and on the other side the physicians were careful not to wound their tender susceptibilities by impertinent questions, yet were determined to get to the bottom of the case and anxious to make effective recommendations. It was evident that courtesy and tact were just as necessary to success in this work as scientific knowledge. In all instances, before the inspection was completed, the families of the patients were carefully advised in regard to the cleaning and disinfection of the infected bed-clothing and wearing apparel and warned of the necessity of immediately isolating any other members of the family who should develop symptoms of illness. Finally, a complete history of the case is written up, embracing the work of the station, of the hospital authorities, and of the district physician, the case is charted at the station and a copy of the history forwarded to the officials at Berlin.

By this very elaborate system the extent and the distribution of typhoid fever in Saarbrücken is worked out to the finest detail, the most accurate knowledge of the bacillus carriers is obtained and the various hygienic measures necessary to stamp out the disease are learned. The sanitary authorities are kept informed of any unhygienic conditions which may be found in the community and measures looking towards the improvement of the water supply, the sewage and garbage disposal are constantly being put in force.

Many interesting details of this great work are related by the bacteriologists connected with the Saarbrücken institute. Some of these indicate the great difficulties of the investigation, while others show the skill with which the authorities have run down their quarry. They illustrate also how tenderly and carefully the population must be handled if results are to be obtained. Early in the campaign, for instance, attention was called to the continued occurrence of typhoid fever in one particular farm-house. The disease was constantly breaking out among the new servants coming to the place while the family of the farmer never seemed to be long free from attacks. During a period of six or seven years as many deaths occurred among the servants or in the farmer's children. A carrier was naturally surmised and suspicion was finally directed to the aged grandmother as being the person in question. All efforts to obtain samples of her urine or stools were fruitless. She stubbornly refused to send any material for examination or what was sent was not believed to be her own. Finally an epidemic of the disease broke out in the vicinity and on some pretext or other the old woman was persuaded to enter the hospital for a few days. Here it was at once established that she was a chronic excreter, her attack of typhoid apparently dating back nearly thirty years.

On another occasion a poor unfortunate bacillus carrier was heard bemoaning her fate to one of her neighbors. Every time her excreta were sent to the station she was informed that she was still "sick" and sick she must remain, an object of suspicion to family and friends. "What a fool you are," said her neighbor. "Just send the dejecta from your daughter and in two weeks you will be perfectly well." And that, of course, is the unfortunate truth.

In thus watching the anti-typhoid work at Saarbrücken and talking intimately with the bacteriologists there my greatest interest naturally lay in getting an expression of opinion from them as to the efficacy of the measures employed and as to the eventual outcome of the movement. They were agreed that the actual amount of typhoid fever in Saarbrücken was constantly decreasing, even though it was difficult to bring statistical evidence to prove this point. The great increase in the number of cases of the disease brought to light by the careful study of the population offset the diminution in number which resulted from their rigorous preventive measures. Their yearly statistics were frequently ruined, moreover, by the appearance of the disease in epidemic form. The actual number of epidemics is becoming constantly smaller, however, and the epidemics, which do arise, are more quickly brought to a standstill. The disseminated typhoid is becoming less common, and more important than anything else the number of bacillus carriers is steadily diminishing. Certain areas in the district also, which formerly were infected with typhoid fever, are gradually becoming free from the disease. In general, the typhoid has disappeared more completely from those areas where the hygienic conditions have been improved, especially where a properly controlled supply of pure water has been obtained, than in those regions where the conditions are still bad.

In Saarbrücken, as in every country where typhoid fever is prevalent, the chronic carriers are the great obstacle to the complete elimination of the disease. They are perfectly well individuals and in the eyes of the government entitled to just as full a measure of freedom and protection as are other individuals. Yet they are a constant menace to family and friends, are viewed with suspicion by the local authorities and are apt to become pariahs in the communities where they dwell. Their fate is a hard one and wise indeed will be the government which will learn to provide for their comfort and happiness and yet rob them of the danger they exert towards the individuals with whom they come in contact. Thus far no measures looking to their segregation have ever been adopted by the German authorities and it is hardly likely that such measures could be passed. It has been suggested that legislation might be enacted forbidding bacillus carriers engaging in any occupation where the handling of food comes into play. Despite the pressure which is constantly being exerted to bring about such legislation, the government has steadily refused to enact it. The problem of the bacillus carrier is not, however, a problem for Alsace-Lorraine alone, but for all countries where typhoid fever exists. Whether the solution of this problem lies in preventive legislation or in the field of specific therapy, the problem must eventually be solved if the disease is to be controlled.

After a visit to a typhoid station and even a brief study of the methods employed and the results obtained, one cannot but marvel at the genius of Robert Koch, who with far-sighted wisdom suggested this new plan of campaign against one of the most devastating of our modern pestilences, at the value of that form of paternal government which listens to the advice of its scientific men and seeks to put in practical operation the plans they may outline, and at the energy and industry of its citizens who devote their lives to carrying out its edicts.

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ON THE SEASONAL VARIATIONS IN THE BACTERIAL FLORA OF THE BALTIMORE CITY WATER.

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During the past two years the Baltimore city water has been subjected to routine examination in the bacteriological laboratory of The Johns Hopkins University. The source of the water supplied to the laboratory is the Gunpowder River by way of the reservoirs of Clifton Park and Lake Montebello. For the same period many samples of water have been collected from the Gunpowder River itself and from its various branches. This source of supply represents only a part of the total quantity of water distributed in Baltimore, the rest being derived from Jones Falls and Lake Roland. In a previous communication,[1] we have called attention to the serious and permanent pollution of the Gunpowder River, its danger to the city and the possibility that the typhoid fever in this community may be associated with the immense amount of fecal material which is constantly being poured into our surface supply. The huge rural population dwelling at various points along the Gunpowder watershed explains clearly the source of this fecal pollution of the river and the occasional appearance of typhoid fever in this population, as pointed out by Price, Stokes, and Rohrer,[2] suggests that at almost any time this fecal pollution may become a typhoid bacillus pollution.

Our observations on the character of the Gunpowder water are indentical with those of Stokes and his co-workers at the City Department of Health, and Stokes and Hachtel[3] have reported a serious contamination of Lake Roland and the small creeks which empty into it. In our previous studies on this subject, it was established that the period during which the typhoid fever in Baltimore was at its height in the season of 1910 was also the period when the pollution of the water supply was greatest. This coincidence, while not a proof that our typhoid is water-borne in character, is very suggestive. At the same time the scattered distribution of the cases of this infection in our city is in harmony with the theory that the disease is to be attributed, at least in large part, to its badly polluted drinking water.

In this investigation of the Gunpowder River the regular methods of counting the colonies on agar and gelatin plates and of determining the presence of *Bacillus coli* by planting Smith fermentation tubes with varying quantities of water have been employed. The results of our work along this line have already been published, and one of us has called attention on a previous occasion to some of the organisms which may be found in the Gunpowder and its tributaries.[4] Recently, during a period of eight months the water varied in character from *badly polluted,* at a time of very hot dry weather, showing a positive presumptive test for *Bacillus coli* in 1/1000 of a cubic centimeter, to *fairly pure,* giving this test only in quantities of 5 to 10 cubic centimeters, the number of organisms on the plates showing corresponding fluctuations. We have therefore attempted to gain further information in regard to bacterial pollution of water by a consideration of the variations in frequency exhibited by the several species from time to time. For this purpose we have poured agar plates regularly from the fermentation tubes in which the presumptive test for *Bacillus coli* was positive, picked out on these agar plates all those colonies which might be regarded as more or less characteristic of the intestinal bacteria, transferred them to agar and made a study of their cultural reactions. The colonies selected corresponded in general to such as are produced by *Bacillus coli,* being slightly raised, grayish white, moist, glistening, with well defined edges. In addition to these, we have also transferred the spreading colonies of *Bacillus proteus vulgaris* and the porcelain-white sticky growths typical of the encapsulated bacteria. We have thus studied practically all varieties of bacteria appearing on our plates except the pigmented and spore-bearing species. After the organisms were seeded on agar a careful investigation was made of the morphology, motility, and tinctorial properties of the various isolations and of their cultural reactions in agar, gelatin, broth, milk, potato, and with dextrose, saccharose and lactose in Smith fermentation tubes. The manner in which dextrose is decomposed was especially observed and the ratio of hydrogen to carbon dioxide was determined with all the fermenting bacteria. These cultural reactions were read at 37° C. except in the case of gelatin, readings being made at the end of 48 hours and 10 days. As far as possible the cultural characters of each isolation were carefully studied, but the attempt was made not so much to work out any particular strain with great detail as to classify the organisms on broad general principles in certain well-defined groups. The following species have been isolated and studied, and their relative frequency at various times estimated.

Bacillus coli Escherich.

This species was present at all times in the Gunpowder water. Only organisms with a characteristic morphology and motility, negative to Gram's stain, producing moist glistening growths on agar, failing to liquefy gelatin, acidifying and coagulating milk, fermenting dextrose and lactose with gas and acid production, the gas in dextrose consisting of hydrogen and carbon dioxide with the formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$ were included. An abundant yellow-brown growth on potato was shown by the majority of the isolations and in general a positive indol test was given.

During the period of greatest pollution *Bacillus coli* could be isolated on nearly every occasion from those fermentation tubes which were planted with 1/100 of a cubic centimeter, and on one

occasion it was obtained in a dilution of 1 to 1000. At that time the agar counts showed from 500 to 2500 bacteria to a cubic centimeter. Of the non-pigmented non-sporebearing colonies which appeared upon the plates, however, only about 25% proved to belong to this type. Subsequently, when the water was comparatively pure, the presumptive test being obtained from 5 and 10 cubic centimeters, with a bacterial count running well under 1000, it was found that this organism comprised over 50% (55%) of the characteristic colonies.

Bacillus cloacae Jordan.

Organisms belonging to this species were encountered constantly in the Gunpowder water. In morphology and motility they resembled *Bacillus coli* except that in general the individual elements were a little larger. Like it they were negative to Gram's stain. On agar they produced a bluish-gray opalescent growth. In gelatin a napiform liquefaction occurred in from one to nine days. Litmus milk was first acidified, then coagulated, and later the precipitated casein was dissolved producing a clear yellowish serum. The carbohydrates, particularly dextrose and lactose were always fermented, and in dextrose the gases evolved showed the inverted formula $\frac{H}{CO_2} = \frac{1}{2 \text{ to } 3}$. On potato the organisms made a rather dirty yellowish or yellowish-brown growth. The reactions for indol were negative.

Representatives of this form occurred at all times, both at the period of greatest fecal contamination when the presumptive test was positive in 1/10 and 1/100 of a cubic centimeter, and in the time of relative purity when 5 and 10 cubic centimeters of water were required to give this test. When the pollution was at its maximum this species comprised about 10% of the intestinal colonies found, while in the period of purity about 25% of the colonies fished proved to belong to this group. It fluctuated in number therefore in much the same way as did *Bacillus coli.*

Bacillus fœcalis alkaligenes Petruschky.

A regular inhabitant of the Gunpowder water is an organism which we regard as *Bacillus fœcalis alkaligenes* of Petruschky. On many of the plates poured from the fermentation tubes were found colonies indistinguishable from those of *Bacillus coli* in size and shape, but usually somewhat flatter and more translucent. When transferred to agar they grew upon this medium in a manner resembling that of *Bacillus coli.* Morphologically they were somewhat longer than this organism however and were actively motile, often growing in chains or threads. They were negative to Gram's stain. They failed to liquefy gelatin, fermented none of the carbohydrates, growing only in the open bulb of the fermentation tube where the reaction was alkaline, and produced an intense alkaline reaction in litmus milk without coagulation. On potato the organisms developed in a grayish-white moist layer. The test for indol was usually negative. The bacteria which we consider *Bacillus alkaligenes* are identical in reactions with the bacteria of the same species which we have frequently found in the contents of the intestinal tract.*

* Some difficulty is always met with in identifying *Bacillus alkaligenes* when isolated from water owing to the resemblance which it bears to certain well-known fluorescent bacteria, especially *Bacillus fluorescens non-liquefaciens*, the cultural reactions of which are almost the same. If the former species happens to be very slow in developing its fluorescent pigment, it may be mistaken for *Bacillus alkaligenes.* The strains which we have identified as the bacillus of Petruschky were kept in the laboratory for from eight to ten months and at no time could a fluorescent pigment be detected.

This species, like the two preceding, occurred constantly in the city water. During the period of greatest pollution it comprised only about 10% of the intestinal colonies however, but at the time of relative purity about 15% of these colonies proved to be *Bacillus alkaligenes.*

Bacillus proteus vulgaris Hauser.

On many occasions spreading colonies were found on the agar plates and when transfers were made the organisms cultivated proved to be representatives of the proteus vulgaris group. Morphologically these organisms were long slender rods with a marked tendency to form threads and chains. They were usually actively motile, but showed the periods of quiescence alternating with periods of activity characteristic of proteus. They decolorised by Gram's method. On agar the organisms produced a slimy, moist, glistening, spreading, rather watery layer. Gelatin was rapidly fluidified with a saccate liquefaction. In milk acid was first shown and usually a soft coagulum. The reaction soon became intensely alkaline and the casein was converted into a clear dark yellowish serum. Dextrose was fermented with the formation of acid and the evolution of a gas with the formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$. On potato the growth was raised and had a dirty yellowish color. In all albuminous media the organisms evolved a disagreeable odor of putrefaction.

This species was found nearly every week in the city water, comprising about 10% of the intestinal forms during the height of pollution, but appearing also in the time of relative purity when about 5% of the colonies transferred belonged to it.

Liquefying Fermenting Organisms.

One of us (*l. c.*) has previously called attention to a peculiar type in the Gunpowder water which bore a close resemblance to *Bacillus coli,* but was easily to be distinguished from it by its liquefaction of gelatin. The individual bacteria in this species were short and plump in form and showed a moderate motility like that of *Bacillus coli* and like the latter species were negative to Gram's stain. The agar colonies were round and circumscribed and on slant agar the organisms produced a moist glistening grayish-white growth indistinguishable from that shown by the bacillus of Escherich. Milk was acidified and coagulated and the casein slowly peptonised. On potato the growth was profuse, a dirty grayish-white layer which later became yellowish-brown. No indol was present. Both dextrose and lactose were fermented, and in dextrose the gas evolved had the regular formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$.

These reactions, with the exception of milk, are thus seen to resemble those of *Bacillus coli,* and a provisional diagnosis of this species was frequently made. In the gelatin tubes the organisms first grew as a delicate white line along the line of inoculation and spread out slightly on the surface of the gelatin at the point where it had been punctured by the needle. After the lapse of two or three days, however, liquefaction of the gelatin occurred and proceeded slowly along the line of inoculation in a saccate form leaving a firm hard base of solid gelatin covered over by the fluidified medium. Frequently a line of bubbles like a string of beads or pearls was seen, extending from the central part of the tube in an upward direction, and

this appearance was often the first indication that liquefaction was beginning. This was found so constantly that we came to regard it as rather characteristic.

These organisms evidently form a distinct and well-defined species. The representatives which we have recently isolated are indentical with some found previously in the various tributaries of the Gunpowder River, in samples of spring water sent to the laboratory for examination, and in specimens of the Baltimore sewage. Occasional obscure references in the literature may be found to bacteria with these reactions and the term "liquefying coli" has been applied to them.[5] The species is easily differentiated from *Bacillus coli* by its liquefaction of gelatin, and it more closely resembles *Bacillus cloacae* than any other organism. We have separated it from *Bacillus cloacae* because of the gas formula, one of the principle cultural reactions of Jordan's bacillus being the production of a gas composed chiefly of carbon dioxide. According to Fuller and Johnson,[6] and Winslow,[7] however, it might be included in the cloacae group.

This liquefying fermenter had a peculiar place in our city water. During the time of greatest pollution it was frequently isolated, fully 10% of the intestinal colonies belonging to this species. It was found in the fermentation tubes which gave a positive test from the smallest quantities of water, from 1/100 and from 1/1000 of a cubic centimeter. Subsequently when the amount of pollution diminished the water becoming relatively pure, these organisms seemed to disappear entirely from our plates.

Bacillus lactis ærogenes Escherich.

A number of strains giving the reactions of the lactis ærogenes group were encountered in various plates poured from the fermentation tubes. Morphologically they were thick, plump, non-motile bacteria, negative to Gram's stain. On agar plates they made heavy, raised, porcelain-white colonies, and on agar slants a raised convex growth along the line of inoculation. Both colonies and slants on agar showed a mucoid consistency with a tendency to string out in fine threads when touched with the platinum wire. In gelatin the organisms developed well along the line of puncture and spread out on the surface as a convex raised porcelain-white knob. The growth on potato was heavy, moist, yellowish-white in color with a strong cheesy odor. Dextrose, saccharose and lactose were all fermented with the production of acid and gas, the gas formula being $\frac{H}{CO_2} = \frac{1}{1-2}$. In litmus milk an abundant acid developed followed by a rapid coagulation. In this medium capsules could be demonstrated in some cases. While we regard the presence of capsules as an essential characteristic for the lactis ærogenes group we have in the present study included not only organisms with the cultural reactions mentioned above in which capsules were actually stained, but a number of isolations with the same reactions in which capsules were not proven. The morphology and lack of motility of the organism and their mucoid colonies of a sticky consistency indicated that they belonged in this group. (See Fuller and Johnson (*l. c.*) and Winslow (*l. c.*).)

The *Bacillus lactis ærogenes* was obtained from the Baltimore city water only during the period of greatest pollution when the presumptive test for *Bacillus coli* was positive in a dilution of 1-100. At this time about 10% of the colonies picked proved to be this organism. Later, when the pollution of the water had diminished in intensity mucoid colonies were no longer found on the plates poured from the fermentation tubes.

Intermediate Group.

On a few occasions we encountered bacilli which could only be placed in the intermediate, Gärtner, or Hog Cholera group. These organisms resembled *Bacillus coli* in morphology and motility, were negative to Gram's stain and produced on agar a moist, rather thin, translucent growth, indistinguishable from that formed by this species. In gelatin the growth was abundant along the line of puncture and on the surface, no liquefaction resulting. In milk a preliminary acidity was observed followed by an alkaline reaction. Dextrose was fermented with a gas formula $\frac{H}{CO_2} = \frac{2 \text{ to } 3}{1}$ but neither saccharose or lactose was acted upon. A yellowish-brown growth was seen on potato, and the test for indol was negative.

Organisms belonging to the intermediate group were found but rarely in the city water except in the height of pollution at which time they formed about 5% of the intestinal colonies.

Attenuated Forms.

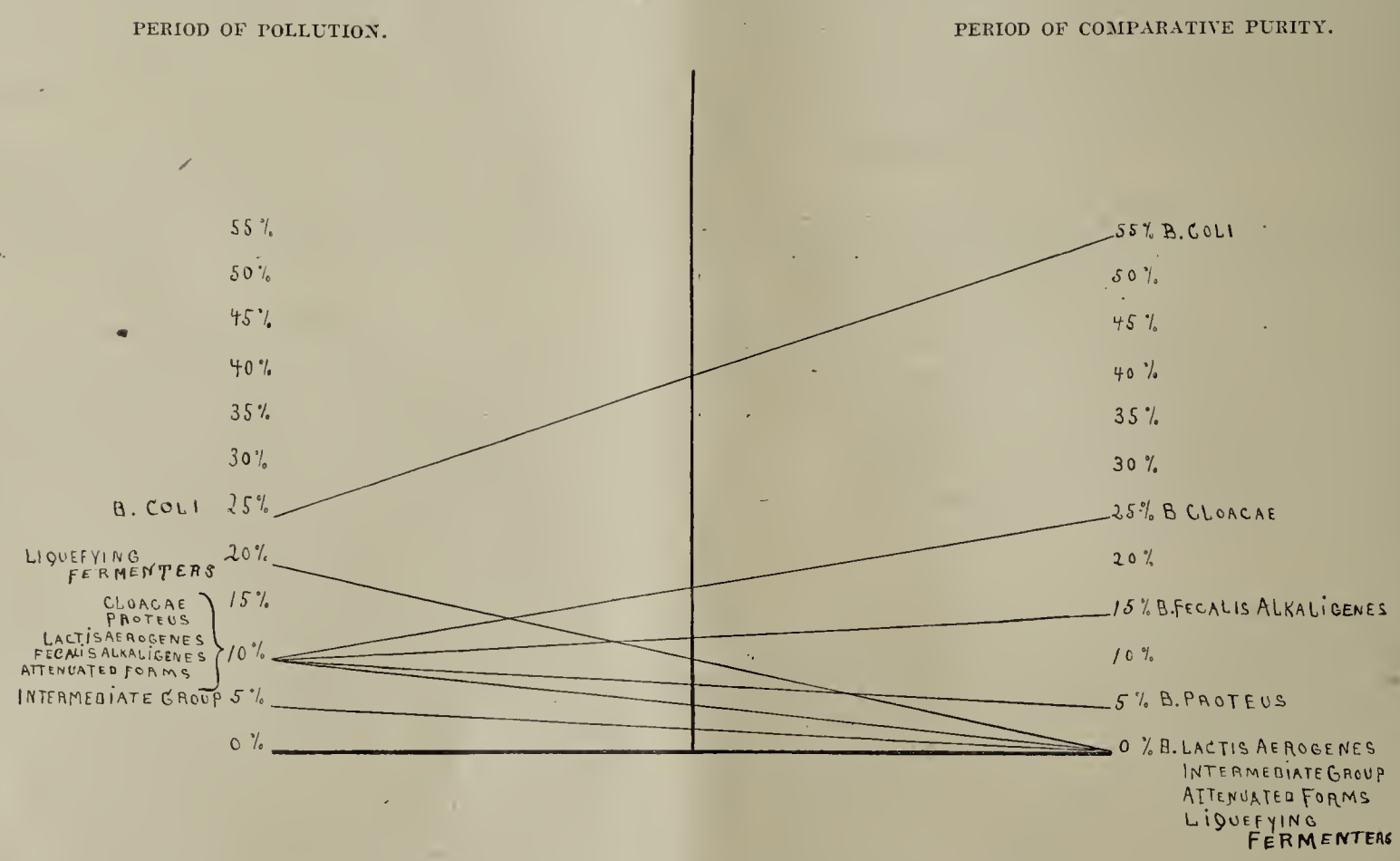
In addition to these organisms with well-defined characters a great many others were isolated from time to time and their cultural properties tested. Many of these turned out to be attenuated forms of easily recognised species. When originally obtained their reactions were inconstant and difficult to interpret. This was especially true in regard to the carbohydrates, which showed merely an acidity with sometimes a bubble or two of gas. By transferring these organisms daily from fermentation tube to fermentation tube their activities were increased so that eventually they caused an abundant evolution of gas. Such cultures could easily be classified after their reactions on the culture media had become fixed, and they were then found to belong to the types of *Bacillus coli, Bacillus cloacae, Bacillus proteus vulgaris,* or to the "liquefying fermenters." The rejuvenated *Bacillus coli* proved to have very constant reactions, the transfers to solid media retaining their properties and continuing to split the carbohydrates vigorously. The proteus and cloacae cultures, however, when grown for some time upon solid media, reverted to their inconstant character, producing but little change in the carbohydrates. At the same time descendents of these strains which were transferred from Smith tube to Smith tube, retained their ability to ferment the sugars actively.

We have placed these attenuated forms together because of their occurrence in larger numbers at the period of great pollution. At the time when fermentation was produced by small quantities of the city water, 1/100 of a cubic centimeter, about 10% of the colonies picked gave these attenuated forms. Later, when the serious pollution disappeared, the organisms isolated were much more fixed and definite in character and presented little or no difficulty in identification, few attenuated forms being encountered.

Discussion.

By reference to the accompanying chart, which represents the relative frequency of the various organisms described above, it may be seen that as the Baltimore city water changed from a condition of extreme pollution to one of relative purity there was a qualitative change in the bacterial flora as well as the quantitative one which has previously been indicated (*l. c.*). It might be expected *a priori*, and on the basis of analogy with the changes which Winslow (*l.c.*) has shown to occur in sewage on storage, that when the filth in the Gunpowder water was concentrated, as in the severe drouth which marked the season when these examinations were begun, the period of high pollution, the bacteria representative of fecal contamination would merely appear in greater numbers. As a matter of fact, the change in the bacterial flora was far more fundamental than this. Organisms were found at the time of pollution which were not usually present in the Gunpowder water, while the bacteria ordinarily found there and indicative of fecal contamination were by no means as frequent as when the supply was good. Thus *Bacillus coli*, always in evidence on the plates, during the height of contamination comprised but 25% of the intestinal forms encountered, while subsequently, when the pollution had passed away, it represented over one-half of the species present, or 55%. The same variation held true for *Bacillus alkaligenes* and *Bacillus cloacae* which rose respectively from 10 to 15% and from 10 to 25%. The relatively smaller proportion of these organisms in this period of pollution is to be explained by the appearance of forms which do not occur at all or so rarely among the bacteria found normally as not to be conspicuous, and by the increase in the members of the proteus group. About 15% of the isolations were found to belong to this latter group while later they fell to 5%. In addition *Bacillus lactis aerogenes* comprised 10% of the colonies, "the liquefying fermenters," 10%, and the intermediate group, 5%. The rest of the forms isolated, about 10%, we have placed in the category of attenuated organisms. With the extreme degree of filth we have then primarily a greater diversity in the intestinal bacteria isolated from the city water. Even if we should disregard the amount of gas and its ratio in classifying the "liquefying fermenters," which would permit them to be placed with *Bacillus cloacae* we would still have the appearance of *Bacillus lactis aerogenes*, the intermediate and the attenuated forms to account for. The frequency of these aberrant types suggests another phase of bacterial growth. Possibly when the fecal material in the water is concentrated the conditions become favorable for the survival and multiplication of certain bacteria brought into the river with the excessive amount of waste material from human or animal sources while under ordinary circumstances, when this material is diluted, such organisms may fail to survive in the struggle for existence with the bacteria ordinarily found in the water. The presence moreover of so many attenuated forms which after prolonged cultivation in the laboratory assume fixed characters, the originals from which they were derived remaining inconstant, indicates that very profound alterations had occurred in the conditions governing the life of the various organisms. The fact that this period of high pollution was also the season when our typhoid fever was at its height raises important theoretical questions as to the epidemiology of this disease. Is it possible that the hot weather of summer can offer better conditions for

Relative Proportion of Organisms.
Baltimore City Water.



the survival and multiplication of the typhoid bacillus in water, as apparently it does offer better conditions for the development of a more diversified fecal flora, than the moderate weather of the spring or fall or the cold weather of winter? With the evidence at hand this can only be suggested as an interesting line of speculation. Finally in view of the fact that the Gunpowder water at the time of extreme pollution reveals the presence in quite large numbers of the bacteria which we have designated as "liquefying fermenters," the question may also be raised whether the occurrence of these organisms in water may not be indicative of its very serious contamination. Further investigation only can settle this point.

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THE MIDWIVES OF ANNE ARUNDEL COUNTY, MARYLAND.*

By Helmina Jeidell, M. D., and Willa M. Fricke, M. D.

In an effort to solve the midwife problem in the United States there have been careful reports published of the midwifery conditions in three large American cities: Baltimore, Chicago and New York. Up to the summer of 1911, however, no investigation of conditions in the rural districts had been attempted. In these the character of the population, the industries and transportation facilities present an entirely new phase of the question. Therefore, an investigation in Anne Arundel County, Maryland, was undertaken under the direction of Dr. Mary Sherwood.†

This county was selected as a fairly typical example of the conditions existing throughout the country districts of the State, with its mixed population, native whites, foreign whites, and colored, and the varied nature of its industries, ranging from farming to oystering and canning. The means of transportation here is almost entirely by horse.

Anne Arundel County lies on Chesapeake Bay just south of Baltimore County and includes the city of Annapolis. It covers an area of 430.4 square miles. A recent census gives a population of 43,740, of which 26,775 are white, 16,965 are colored. The county is divided into eight election districts, in each of which there are usually two Board of Health subregistrars who report to the local registrar at Annapolis. All but two of the registrars are physicians. Outside of the city of Annapolis there are twenty physicians, or approximately one physician to every twenty-one square miles.

Before presenting the details of the investigation which we have conducted in this county, it may be well to give a brief summary of the requirements in this State for the licensing of midwives:

1. If in actual practise prior to July 1, 1910, a license will be issued without examination after registration with the local registrar.

2. After July 1, 1910, requirement for registration and license is the passing of an examination with the State Board of Health; applicants for examination must be qualified to read and write, must be able to fill out correctly the required birth certificate and present a certificate from a maternity hospital or legally qualified practitioner of applicant's attendance on at least five cases of childbirth, and that such applicant is competent to attend ordinary cases of labor.

The statute declares it unlawful for any midwife to make a vaginal examination, to attempt to deliver a retained placenta, to use forceps, to attempt version or any forcible delivery, and requires that in all cases of labor not normal a licensed practitioner be notified.

Report of all cases of ophthalmia neonatorum is obligatory.

We are under great obligations to Drs. Price and Beitler of the State Board of Health for their hearty co-operation and assistance. From them we obtained a list of the registered midwives. Owing to the difficulties of traveling in the county, we found it convenient to fix our headquarters in Annapolis and make trips of several days duration into the various districts where the registrars cordially gave us invaluable assistance in locating the midwives in their vicinity. Many of the houses were difficult to reach as they were miles away from the main road. In conducting the interviews with the midwives we used the questionaire prepared by the Committee on Midwifery which is similar to that employed in all previous investigations, and a tabulation of the facts obtained was prepared which appears in Tables I and II.

Of the 119 midwives practising in the county 17 or 14.28% are Americans, 95 or 79.83% are colored and 7 or 5.71% are foreigners, including 2 Germans, 2 Poles, 1 Lithuanian, 1 Bohemian and 1 Dane. Twenty are practising in the city of Annapolis.

The white midwives take only white cases. The colored midwives take white and colored cases, and the latter they deliver themselves, whereas to most of the white cases they serve only as obstetrical nurses with a physician. Three of the 119 midwives had about 75 cases a year; 1 had 65; 2 had 50; 2 had 35. The remainder averaged from 3 to 30 cases a year.

Two-fifths of the births in Anne Arundel County recorded at the Health Department are attended by midwives. In the year 1911 40% of this two-fifths were reported by three midwives. Only 33 of the 119 midwives state that they ever report births, and most of these do so only occasionally.

* This study was made possible by the generosity of the Maryland Society for the Prevention of Blindness.

† Chairman of the Committee on Midwifery of the Association for the Study and Prevention of Infant Mortality.

Of the 119 only 4 had been trained in a school for midwives. The remainder were self-taught or had worked with a physician at the bedside. One of the 4 had attended a school for midwives in Chicago for six months. Two had a six months' hospital training, one in Germany, one in Russia. One had two and a half years in a hospital in Denmark. Two colored midwives had "responded to the call of a good spirit."

Thirty-four had registered with the Board of Health; 21 of these had received licenses to practise. Only 3 had signs displayed according to the law. Seventy-seven could neither read nor write.

Practically all the midwives made vaginal examinations. All professed to wash their hands with soap and water although, according to the physicians, many go unwashed directly from field labor to an obstetrical case. A number lubricated their hands and the vulva with lard or vaseline. Only 2 of the 22 who claimed to use antiseptics had any comprehension of their significance. Prophylactic silver nitrate was used by no one. Seventy-four attended normal cases only. Forty-five called in no medical assistance even for such complications as hemorrhage, retained placenta and abnormal presentations requiring version. Perineal tears were apparently not recognized at all, but three admitted their occurrence. One alone of the 119 midwives carried a bag with the requisite supplies and that was not clean. Some sort of a bag was carried by 31—the usual equipment being vaseline, a ball of twine and scissors. One displayed a pair of gilt nail-scissors with especial pride; 4 carried thermometers. The midwives did not count the pulse; 1 colored midwife stated that she always felt the pulse, but gave as an estimate of the normal pulse, "about two."

The fees received average from $3 to $5, although several of the white women earn as much as $10 to $25. The distances to be traveled often make it necessary for the midwife to remain at the home of the patient. In these cases, besides the confinement and nursing, her duties always include entire charge of the household. Many, however, make daily visits for ten days toiling backward and forward several miles over the country roads.

TABLE I.—119 MIDWIVES OF ANNE ARUNDEL COUNTY—PERSONAL STATISTICS.

Nationality.	Number.	Age in Years.								Residence in America.				Education.				Diploma.			License.		Registered at Health Board.		Home Conditions.			
														Read and Write.		Speak English.												
		20 or less.	20—29.	30—39.	40—49.	50—59.	60—69.	70—79.	80—89.	1 yr. or less.	1—10 yrs.	10—20 yrs.	20 or more.	Yes.	No.	Yes.	No.	American.	Foreign.	None.	Yes.	No.	Yes.	No.	Good.	Fair.	Bad.	Not seen.
Americans	17	..	..	3	4	8	1	1	..	..	..	..	..	14	3	17	..	1	..	16	1	16	3	14	12	3	1	1
Negroes	95	..	..	6	19	42	16	10	2	..	..	..	..	12	73	95	..	..	..	95	18	77	29	66	20	62	9	4
Germans	2	..	..	..	..	1	1	..	..	..	1	1	..	2	..	2	..	..	1	1	..	2	..	2	1	..	..	..
Bohemians	1	..	..	1	..	..	..	..	..	..	..	..	1	1	..	1	..	1	..	..	1	..	1	..	1	..	..	..
Dane	1	..	..	..	..	..	1	..	..	..	..	..	1	1	..	1	..	..	1	..	1	..	1	..	1	..	..	..
Lithuanian	1	..	..	..	..	1	..	..	..	..	..	..	1	1	..	1	..	..	..	1	..	1	..	1	1	..	..	..
Poles	2	..	..	..	..	1	1	..	..	..	..	2	..	1	1	..	2	..	..	2	..	2	..	2	1	1	..	..
TOTAL	119	..	..	10	23	53	20	11	2	..	1	3	3	32	77	117	2	2	2	115	21	98	34	85	37	66	10	5

TABLE II.—119 MIDWIVES OF ANNE ARUNDEL COUNTY—FACTS ABOUT THEIR PRACTISE.

Nationality.	Number.	Length of Practising Years.				Methods of Practice.																		Care of Infant's Cord.				Attention to Mother.		Suspected of Criminal Practise.	Receives and Cares for Patients in Home.
						Attends Normal Cases Only.		Uses Antiseptics.			Equipment and Cleanliness of Bag.				Care of Infant's Eyes Bathed Daily.				Prophylactic (Boric)											
		1 or less.	2—9.	10—19.	20 or more.	Yes.	No.	Yes.	No.	Sometimes.	Fair.	Bad.	Not seen.	None.	Boric.	Water.	Breast Milk.	No.	Yes.	No.	Twine and Powder or Nutmeg.	Twine and Absorbent Cotton.	Twine and Lard or Vaseline.	Sterile Tape and Aseptic Powder	Yes.	No.		
Americans	17	1	4	18	4	14	3	8	7	2	..	4	..	13	9	6	1	1	7	10	9	1	2	5	17	..	1	..
Negroes	95	1	19	36	39	59	36	10	71	14	..	24	..	71	21	55	3	16	8	87	28	7	57	3	89	6	1	1
Germans	2	..	..	1	1	1	1	1	1	..	1	..	..	1	1	1	..	..	1	1	..	..	1	1	2	..	..	..
Bohemians	1	..	..	1	..	1	1	1	..	..	..	1	..	..	1	..	..	..	1	..	..	..	..	1	1	..	..	..
Dane	1	..	..	..	1	..	1	1	..	..	..	1	..	..	1	..	..	..	1	..	..	..	..	1	1	..	..	..
Lithuanian	1	..	..	1	..	..	1	1	..	..	..	1	..	..	..	1	..	..	..	1	..	..	1	..	..	1	..	..
Poles	2	..	..	..	2	..	2	..	2	..	..	..	..	2	..	2	..	..	..	2	..	..	2	..	..	2	..	..
TOTAL	119	2	23	47	47	74	45	22	81	16	1	31	..	87	33	65	4	17	18	101	37	8	63	11	110	9	2	1

A history of puerperal infection, criminal abortion and ophthalmia neonatorum is quite impossible to obtain. According to one of the physicians Neisser infection was very uncommon until, within recent years, the electric lines and State roads have made communication with the city easier. Only two midwives were suspected of criminal practise, and these were white. According to the physicians it is the patients themselves who induce abortion.

The country midwife labors under peculiar difficulties. She is not trained to recognize complications early and when emergencies arise it may take hours before a physician can arrive. One case of post partum hemorrhage was lost by a colored midwife who had been impressed by a doctor that under no circumstances must she introduce her hand or anything else into the birth canal. When the hemorrhage com-

menced she sent five miles to the nearest doctor who happened to be in attendance on a case three miles from home in a house where there was no telephone. That midwife is held in ill repute in the neighborhood because she refused to treat the complication herself. Those who assume any responsibility and are most officious—usually the white midwives—are the most popular. One of this type naïvely stated that she always removed the placenta manually, immediately after the birth of the child, because she thought it was so much better for the mother. She also repaired perineal tears.

The colored midwives are spoken of as "grannies." The plane on which they are held is shown by the fact that when they are too old for any other work they become midwives. For the most part the colored midwife attempts less than the white and her practise is, perhaps, more easily guided by the physician, whereas, the white midwife has much more initiative and is more likely to compete with the physician for obstetrical cases.

The white midwives who have the largest practises and receive the highest fees live in or near the towns.

The following are some of the practises of a few colored midwives:

1. *Treatment for hemorrhage.*—Ice held in the hand; licking alum; a hot potato held in the hand; equal parts of paregoric and laudanum by mouth while at the same time a piece of cloth is burned in the stove; packing the vagina with any kind of rags that are handy in case of post partum bleeding.

2. *Treatment for delayed placenta.*—Feathers burnt under the nose of the patient to make her sneeze; salt held in the hands to make them sweat while the patient blows into a bottle.

3. *The use of douches and ergot.*—In one neighborhood ante partum douches were routine. Post partum douches are quite commonly used when the placenta is not intact or when the lochia have an abnormal odor. The midwife carries from patient to patient her own douche tip, which she greases before using. Ergot is used by a few of the white midwives to increase labor pains.

4. *The kinds of pads used.*—Anything from greased rags to burlap is used by the very poor unless the midwife is in a position to furnish them with something different. On one occasion we visited a poor Lithuanian woman who had been delivered that morning in a room containing two dilapidated beds and a broken chair. The midwife whom we accompanied informed us that a woman washing at a tub whom we could see from the window, had been confined the day before in the other bed. Our midwife not only received nothing for these confinements but even supplied these poor women with clean pads.

In our interviews we marveled at the intelligence of several of these colored midwives who had their training on plantations before the war and who to most of our questions gave replies which would have been a credit to the present generation. They formed a pleasant contrast to the one who in response to our request to see her license amiably produced her marriage license. Notwithstanding their superstition and ignorance the colored midwives were on the whole a simple-minded, sympathetic lot ready to trudge miles over the sandy roads in the midsummer heat to earn their meager fees which in many cases they never received at all.

In conclusion we feel that in the southern rural districts there is a special problem to solve. Most of the physicians in the country agree that the midwife cannot be dispensed with. The distances are too great for the number of physicians practising there and yet the fees are too small to support a greater number of physicians. Since the midwife seems to be a necessary evil in these southern districts the problem resolves itself into one of education. Yet unless the training and equipment were provided gratis the average colored midwife could not avail herself of it. Having had it would she be willing to continue to receive so small and uncertain a remuneration? At the present time the local physician must be looked to not to solve the problem, but for the palliation of these lamentable conditions and to encourage him there is demanded a closer supervision of the midwifery conditions existing in his community.

NOTES ON NEW BOOKS.

The Care of the Skin and Hair. By William Allen Pusey, M. D. (*New York and London: D. Appleton & Co., 1912.*)

This is a small book which can both with safety and profit be put in the hands of the laity. It contains much good advice, which if followed will save the pocketbooks of many seeking relief at the hands of quacks and beauty restorers. Dr. Pusey has written a book which is simple and has an attractive style adapted to the needs of the average intelligent reader.

Text-Book for Nurses: Anatomy, Physiology, Surgery and Medicine. By E. W. Hey Groves, M. S., F. R. C. S. and J. M. Fortescue-Brickdale, M. A., M. D. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

The teaching of nurses, like the teaching of other classes of students, is not as yet well fixed along different paths, some instructors being anxious to give these women much more instruction than others think suitable. Up to a certain point the more nurses get the better as it thus fits them to fill creditably the many new fields of work that are opening to them. But when it is to be decided just how much anatomy or physiology is to be taught them, much depends on the teacher and the number of hours that are to be given to the subject in the school curriculum. This new text book of about four hundred large pages comprises the instruction in four fundamental subjects; eighty devoted to anatomy; somewhat less to physiology; nearly one hundred and fifty to surgery and less than one hundred to medicine. To the reviewer these proportions seem incorrect, for he feels that nurses have a greater need of thorough training in physiology and medicine than in anatomy and surgery, but so far as what the authors have to say on these four subjects, they have written a useful book. The subjects are treated simply but in a comprehensive way so as to give a nurse a good grasp of the branch she is studying. As the preface states: "The chief aim . . . . of the present book is to enable the nurse to understand the principles

underlying the medical and surgical treatment which it is her duty to assist in carrying out," and the authors have reached their goal in a satisfactory manner. It is hardly to be expected that this English work will be a standard text-book in any one of the American schools of nursing, but it is one which should be in the library of all such schools for nurses to refer to and study, for it is reliable and well written.

Stomatology in General Practice. A Text-Book of Diseases of the Teeth and Mouth for Students and Practitioners. By H. P. Pickerill, M. D., etc. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

In this work the author has bridged over a "somewhat ill-defined territory lying between medicine and dentistry, which to many practitioners is to a certain extent a *terra incognita.*" There is no doubt that this territory exists, and its recognition has led of late to the establishment of dental clinics in a few hospitals, and it is to be hoped that the number of these clinics will be rapidly increased. But where no clinics exist this book will be most helpful to both students and practitioners, especially surgeons, for the author is not only a skilful operator in difficult cases dealing with the teeth and jaws, but he also has written the kind of text-book which is needed by the profession; in other words it is well balanced and the pure internist, as well as the general surgeon, will benefit by its perusal. Dr. Pickerill describes inflammatory diseases of the mouth, the manifestation of systemic diseases in the mouth, oral sepsis and its effects, the relationship of oral disease to various lesions of the nervous system, caries of the teeth and its prevention, the surgical treatment of dental disease, fractures, dislocations, and closure of the jaws and oral tumors. These chapter headings indicate the general scope of the work, which is not too large, or covers too much ground. "Stomatology in General Practice" may be cordially recommended to those eager to have a good understanding of the troubles described.

Electrical Injuries: Their Causation, Prevention and Treatment. Designed for the Use of Practical Electrical Men. By Charles A. Lauffer, M. D. 50cts. (*New York: John Wiley & Sons, 1912.*)

This little first-aid volume may assist electricians who are liable to burns or shocks from highly charged electrical apparatus, and also physicians who have not had the opportunity to learn how to treat electrical accidents, but it is a trifling work and padded with matter which has but slight connection with the subject under discussion.

Manual of Surgery. By Alexis Thomson, F. R. C. S. Ed. and Alexander Miles, F. R. C. S. Ed. Vols. II and III. Regional and Operative Surgery. Fourth Edition. (*Edinburgh, Glasgow and London: Henry Frowde and Hodder & Stoughton, 1912.*)

As a manual for students this surgery will appeal to a large class. The many chapters are well proportioned, the directions for operations are clear, and the illustrations serviceable; the size of the volume is such as to make it easy to carry about with one and the type is pleasing. These are all qualities to hold the reader. As an example of what a manual should be, this one ranks high and the authors are to be congratulated on having prepared so excellent a volume.

International Clinics. Vol II. 22nd Series. $2. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

A Symposium on Anaesthesia is doubtless the chapter in this volume which will be most extensively read, but there are other interesting shorter papers by Jackson, one of the very few really skilful operators with the bronchoscope in America, on "Direct Methods of Examination of the Larynx, Trachea, etc," and one by Baruch, who is an authority on hydrotherapy, on "The Management of Sunstroke—A Lesson in Hydrotherapy." Flexner's "Lecture on the Present Status of Epidemic Poliomyelitis" is also one to appeal strongly to the general practitioner.

No. 50. Scientific Memoirs. By Officers of the Medical and Sanitary Departments of the Government of India. *Preliminary Report on an Investigation into the Etiology of Oriental Sore in Canbay.* By Capt. W. S. Patton, M. B. Price 6 annas. (*Calcutta: Superintendent Government Printing, India, 1912.*)

The author after a careful investigation of sixty cases believes the Oriental Sore to be transmitted by the *Cimex rotundatus,* which fact, if proven by further investigations, will add another disease to the growing list of infections due to the bite of various insects.

Primary Malignant Growths of the Lungs and Bronchi. A Pathological and Clinical Study. By I. Adler, M. D. $4. (*New York: Longmans, Green & Co., 1912.*)

Dr. Adler, after a careful search through the literature for the accounts of these growths, has prepared an important contribution to their history, of service both to physicians and surgeons. Only a small part of the volume is devoted to the pathology and clinical symptoms of the tumors, the remaining two-thirds being taken up by an exhaustive analysis of all the cases so far reported. Of these by far the larger number are carcimomata which outnumber the sarcomata by more than 4 to 1. The author has tabulated 375 of the former and 90 of the latter. Besides these there are 100 which are of doubtful origin, and 18 classified as miscellaneous. As a collective report on these oftentimes obscure growths this volume will serve as a most useful guide. As a piece of book-making it is unfortunately not so praise-worthy—it is printed on too heavy paper, and might have been reduced in size so as not to be so expensive.

The Medical Diseases of Children. By Reginald Miller, M. D. (Lond.), etc. 12/6. (*Bristol: John Wright and Sons, Ltd., 1911.*)

It is a difficult undertaking to discuss with entire satisfaction the medical diseases of children in a volume of this size.

The author's concise style has, however, enabled him to produce a small book of real value. It is practical, well illustrated and generally in keeping with the accepted facts and theories of modern teaching.

A few rather positive statements are made which would seem open to argument, for instance, that curd indigestion offers the greatest stumbling-block to artificial feeding and that the use of citrate of soda is the most effectual method of controlling this. For many years the digestion of the fats of cows' milk has been considered quite as difficult and more recently the work of Finkelstein has forced upon us the important and at times disastrous effect of sugars. The experience in this country, at least in the use of citrate of soda, has been generally disappointing. The arrangement of the book is in some respects unique—especially with regard to infectious diseases. The author, as far as possible, has attempted a classification based on the broader conception of the infecting organism, including under tuberculous infection the various manifestations of this disease, under pneumococcal infection, pneumococcal pneumonia, pleurisy, empyema, pericarditis, endocarditis, meningitis, otitis, peritonitis, etc., under the rheumatic infection, acute rheumatic fever, chorea, etc.

While necessarily incomplete in our present knowledge of bacteriology, such a classification is of particular value in connection with children's diseases in emphasizing, as the author states, the tendency toward generalization by bacterial infections in children.

The work throughout has the stamp of one writing from a wide personal experience and can be freely recommended to students and practitioners.

R. A. U.

Oxford Medical Publications. Salvarsan in Syphilis and Allied Diseases. By J. E. R. McDonagh, F. R. C. S. $3. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

As a supplement to the System of Syphilis, in five volumes, under the editorship of Power and Murphy, published a short time since by the Oxford Press, the present volume has been prepared, and makes a fitting ending to the exhaustive and excellent system. McDonagh has had a large experience with the use of salvarsan and his advice is sound, though we cannot agree with him in thinking that primary chancres should be excised when possible. This treatise presents clearly but briefly the general principles underlying the administration, use, and results of salvarsan, and the general practitioner will find it a helpful guide.

Psychotherapy. By James J. Walsh, M. D., etc. $6. (*New York and London: D. Appleton & Co., 1912.*)

There is much in this large volume to help the general practitioner and much that would help patients if presented under slightly different form. The book is a treatise on mind-cure, as exercised by the patient on himself, under the influence or suggestion of his physician. This is a form of cure to which, unfortunately for the patient, few physicians give the necessary time and, therefore, many a patient falls into the hands of quacks, or becomes a confirmed neurasthenic or worse, a burden to himself and his friends and the world about him. Dr. Walsh, after an introduction on psychotherapy in the history of medicine, discusses general psychotherapeutics in four chapters under general considerations, the individual patient, general principles, adjuncts and disturbing factors. He then takes up special psychotherapy as applied to diseases of the digestive tract, heart, lungs, gynecology, skin diseases, etc., and after dealing with the bodily functions, discusses disorders of the psyche under psychoneuroses, disorders of mind and will, and concludes his work of nearly eight hundred closely printed pages with a chapter on psychotherapy in surgery. As can be seen from this incomplete outline the author has attempted to cover nearly all medicine, and while he has written a work of real value from many points of view, with his usual skill and attractive style, yet the work is longer than it need be. There is much repetition as is inevitable in composing such a volume, for suggestions that will help a patient in one disease are in most instances the same as will help him in another disorder, so that it seems hardly worth while to divide psychotherapy into so many sections as the author has done. There are many points to which exception might be taken, but as they do not really affect the value of the work, they may as well be left unnoted, except to indicate that the work is written by an excellent general practitioner who draws more from his own experience than from the more exact conclusions that are being arrived at by the best students of psychology and psychiatry. "Psychotherapy" is a work which fills excellently a hole that has remained empty up to now on the doctor's bookshelves and should be found in every practitioner's library if only to call his attention constantly to this form of therapeutics, which is the best of all in many cases.

Progressive Medicine. Edited by Hobart Amory Hare, M. D., assisted by Leighton F. Appleman, M. D. Vol II. (*Philadelphia and New York: Lea & Febiger, June, 1912.*)

This volume deals with hernia, the surgery of the abdomen exclusive of hernia, gynecology, diseases of the blood, spleen, thyroid gland, nutrition, lymphatic system, and diathetic and metabolic diseases and ophthalmology. It is always interesting to note the amount of literature on hernia, such an ancient topic, and one which would appear as fairly well settled, and yet which so constantly demands fresh consideration. Very naturally cancer of the uterus takes up more space in this volume than any other topic, since there are so many questions in regard to it that remain to be solved. The various chapters are carefully prepared and the few illustrations well chosen.

At the request of Messrs. John Wright & Sons, Ltd. (Bristol, England), we desire to state that they have disposed of the American Market for Dr. Herbert French's Index of Diagnosis to Messrs. William Wood & Co., of New York. We regret that the American publishers did not receive credit for this in our notice of the work in the May issue of the Bulletin.

Die experimentelle Bakteriologie und die Infektionskrankheiten mit besonderer Berücksichtigung der Immunitätslehre. Von Dr. W. Kolle und Dr. H. Hetsch. Dritte, erweiterte Auflage. $8.50. (*Berlin and Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

The third edition of this text-book of Kolle and Hetsch deserves more than a passing notice for a number of reasons. It is in many ways the most comprehensive of the German text-books in Bacteriology and the 1911 edition has been brought thoroughly up to date, including possibly the most of the important advances in the knowledge of this subject which have been made since the appearance of the earlier edition. Its two volumes, comprising together nearly a thousand pages, make it too voluminous and detailed for any but advanced students in bacteriology, and the book, therefore, must be regarded as peculiarly fitted for special workers in this field. The form or arrangement of the material presented is unique. Each special topic is considered in a lecture (*Vorlesung*), there being altogether fifty-nine of such lectures. These vary in length from five to twenty-five pages depending upon the nature of the subject, special lectures being devoted, for instance, to the antitoxins, to the cytotoxins, to methods of serum-diagnosis, and to the principal infectious diseases—anthrax, cholera, typhoid fever, dysentery, malta fever, meningitis, etc. The book is not merely bacteriological in scope, however, since the second volume takes up such diseases as diphtheria, tuberculosis and the protozoan infections, including amoebic dysentery, trypanasomiasis, malaria, and Texas fever. In addition a number of diseases of unknown etiology, such as rabies and small-pox, are considered in detail with an accurate discussion of the several theories which have been advanced to explain their etiology.

Despite the excellent arrangement of the material presented and the careful discrimination which the authors have employed in the selection of the subject matter, in certain particulars the book deserves severe criticism. Throughout both volumes there is an almost absolute disregard of the work of American investigators. In consequence some of the most notable advances in bacteriology and epidemiology of the past few years have not been mentioned. Thus in the chapter on leprosy nothing is said as to the cultivation of the leprosy bacillus by Musgrave and Clegg and by Duval, and in the bibliography attached to this chapter the names of these investigators do not appear. On page 468 of Volume I the definite statement is made that "the cultivation of the leprosy bacillus has not yet been accomplished," and yet the authors have had at least two years to find out about this most important work. Again, slightly less than a page is devoted to typhus fever and no reference is made to the wonderful achievements of Ricketts, Anderson, and Goldberger in Mexico and of Nicolle in Tunis upon the production of this disease in apes and upon the rôle of the body louse in the transmission of the infection from person to person. If the short period of time which has elapsed since the publication of this work and the ap-

pearance of the third edition of Kolle and Hetsch may be put forward as an excuse for the failure of the authors to take account of the recent discoveries on leprosy and typhus fever, the same excuse cannot be used in regard to the failure to mention MacCallum and Opie in the chapter on malaria and Councilman in the chapter on small-pox. While such errors can be regarded as errors of omission, no justification, whatever, can be proposed for the adoption of Fraenkel's name, *bacillus phlegmones emphysematosæ*, for the *bacillus ærogenes capsulatus* of Welch and Nuttall and the statement that this organism was more accurately described by Fraenkel than by the American bacteriologists.

These are but a few examples of the many failures in Kolle and Hetsch's text-book to recognize work done on this side of the Atlantic Ocean, but they serve to indicate how the neglect to carefully review American literature has permitted the introduction of serious errors in the subject matter of which the two volumes are composed. One wonders, indeed, whether the authors are not actuated by the desire to Germanize the entire science of bacteriology, since one reads with surprise on page 852, Volume 2, of the work of "Brinckeshoff and Tyzzu" in Manila only to realize that these names refer to two well-known members of the staff of Harvard University.

Despite these mistakes in this publication, which we feel compelled to mention out of loyalty to American science, the work is thorough, comprehensive and well arranged, the subject matter is carefully chosen, and the two volumes will appeal deeply to all thoughtful students of bacteriology and protozoölogy.

A Manual of Materia Medica for Medical Students. By E. Quinn Thornton, M. D. $3.50. (*Philadelphia and New York: Lea and Febiger, 1911.*)

This is an excellent work which takes up what is usually regarded as rather a dry subject in a clear way. Particularly valuable are the sections on the methods of administration of drugs. The work deals only with the preparations which are in the United States Pharmacopeia and it is a question whether some additions would not add to the value of the book. For example, under digitalis it would be an advantage to find some reference, which need not be extensive, to preparations other than those in the pharmacopeia. It is not always easy for the student to know where to search for information regarding digipuratum, for example. Some of the preparations of arsenic might be cited as another example of this. Doubtless the author considered this and had good reasons for his decision. Perhaps it might be difficult to know where to draw the line and decide what was worthy of mention. One point caught the reviewer's attention, namely, the description of the composition of Blaud's pills. This is given as consisting of carbonate of iron and excipients only. This mistake occurs in several American text-books. The special value of Blaud's mass is that it is a combination of potassium and iron which seems to be more efficient than the iron alone. This is a small matter but the mistake is so common that it is worth drawing attention to it. We can heartily recommend this work as an excellent text-book on materia medica.

Immunity. Methods of Diagnosis and Therapy and their Practical Application. By Dr. Julius Citron. Translated and edited by A. L. Garbat. Illustrated. $3. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This work is intended "to serve a purely practical purpose"; to review briefly "in a purely critical form the various methods of immunity diagnosis, especially those relating to tuberculosis and syphilis." This aim it very well fulfils. The extensive experience of the author both in the laboratory and in the clinic enables him to sift out the essential facts, and to indicate their significance and relative importance. The various laboratory methods of serum diagnosis are simply and briefly explained, in all their essential details. Especially commendable is the emphasis laid on the necessary control experiments. In addition the theories forming the basis of the various tests are critically discussed, but perhaps too briefly.

While intended primarily for the laboratory worker the book should also be helpful to the practising physician in explaining the significance of the reactions and in pointing out just what conclusions may be drawn from positive and negative reactions. The chapters on tuberculin are of special interest. Consideration is given both to its therapeutic and diagnostic use, and the contraindications are carefully outlined. The therapeutic use of sera and vaccines is also briefly considered.

The chief criticisms to be offered are that in places the text is too brief for clearness; that the English at times is a little involved, and that too much of the German idiom has been retained in the translation.

The work is an excellent one and should prove to be of great practical value.

P. W. C.

Parasitic Amœbæ of Man. By Charles F. Craig, M. D., Captain Medical Corps, United States Army. From the Bacteriological Laboratory of the Army Medical School, Washington, D. C., and the Rockefeller Institute for Medical Research, New York City. $2.50. (*Philadelphia: J. B. Lippincott Company, 1911.*)

This volume is a splendid addition to our medical literature and is probably the best treatise in English on a much neglected, but equally important, subject. A brief historical resumé shows how recent is our knowledge of amœbiasis; one notes that Osler is mentioned as the first clinician in America to observe amœbæ in a case of dysentery, in 1890; while to the monograph of Councilman and Lafleur is ascribed much of the stimulus for work on the subject subsequent to the year 1891. Three chapters cover well the biology, nomenclature, classification, and methods for the indentification of amœbæ in general; adequate space is given over to the details of fixation and staining, though for the routine purpose of diagnosis, the value of the examination of fresh specimens, supplemented by intravitam staining with neutral red is well emphasized. The following chapter goes to uphold the author's view "that the parasitic amœbæ of man have not been cultivated."

About 130 pages are then rightly devoted to a minute description of those amœbæ suspected or convicted of causing dysentery in man; namely, the entamœba coli, histolytica and tetragena, and an excellent summary gives in tabulated form those diagnostic points which should enable any careful observer to differentiate the three forms. This is an extremely important thing, not least of all from the stand-point of therapy, when we realize that "if the entamœba coli were the cause of a form of dysentery, practically 50 per cent of all individuals in nearly every locality would suffer from this disease." That the entamœba histolytica *is* the cause of true amœbic dysentery is well emphasized in the section describing the pathology of the disease. Further evidence is advanced to show that the less well known entamœba tetragena and the more recently described paramœba hominis may be blamed for some true cases of dysentery. Several other forms of intestinal amœbæ are briefly mentioned, but the validity of their rights to be classed as distinct pathogenic forms is, in all instances as yet, doubtful. Amœbæ of the mouth, genitourinary tract, exudations, abscesses, and of the lungs, are concisely dealt with. A list of 122 references completes the work, which is excellent as regards printing, illustrations, and a singular absence of typographical errors.

The book will undoubtedly prove of immense value to biologists, workers in clinical laboratories, and to all students in the field of internal medicine.

The Growth of Bone: Observations on Osteogenesis. An Experimental Inquiry into the Development and Reproduction of Diaphyseal Bone. By William Macewen, F. R. S. Glasgow. $2.25. (*James Maclehose and Sons, 1912.*)

This book in an extremely interesting attack on one of the generally accepted tenets of surgery, the belief that periosteum is the essential factor in the reproduction of adult bone, and that diaphyseal bone denuded of its periosteum will die. In the preface, the author states his purpose to show this belief to be fallacious, and the whole volume is a narrative of many clinical cases of great interest, supported by a large number of experiments, all bearing more or less closely on the point at issue.

Macewen holds that bone formation is the result of the life process of the osteoblast, that the adult osteoblast may, under stimulating circumstances, such as fracture or inflammation, regain its embryonic activity, and that when it does so, it possesses at least as great vegetative powers as the epithelial cell. Hence any fragment of bone containing living osteoblasts may become a center of new bone growth, and bone is, therefore, an esaily transplantable or graftable tissue. But the writer holds that normal periosteum contains no osteoblasts, and hence has no power or influence whatever in the regeneration of bone. He grants that when osteomyelitis occurs, the periosteum displays bone-forming ability, but explains it thus: The inflammatory process causes a proliferative reaction on the part of the osteoblasts, which are crowded outward into the periosteum. Were the periosteum not present they would invade the surrounding soft parts and cause an osseous infiltration of muscles, etc. Hence periosteum, instead of being a bone-forming structure, is really a limiting membrane, which checks bone over-growth. When it has become itself infiltrated with osteoblasts as a result of pathological processes, and is then stripped up or transplanted, it displays the power of regenerating bone, but such a power is absent in the case of normal periosteum. Numerous experiments and clinical citations make one feel that the author is well sustained in his contention.

On critical reflection one is led to feel that Macewen's point of view is, perhaps, not so revolutionary as it appears at first sight. His consideration of the whole subject is based on the definition of periosteum as the outer layer of fibrous tissue, connected with the bone proper by loose areolar tissue and free from osteoblasts normally in adult life. While such a definition may be histologically correct, there is no doubt that the surgeon in dealing with what he considers periosteum, and using considerable force to detach it with a semi-sharp instrument, must remove more than Macewen's layer. In fact, in certain of Macewen's experiments where transplanted periosteum developed nodules of bone, he explained that occurrence by the fact that probably a minute flake of bony tissue had been removed with the periosteum. There can be no doubt that periosteum, as removed clinically, frequently contains such particles of bone. Hence one can hardly attach to the conclusions of Macewen the extensive clinical weight they might otherwise deserve.

The book is illustrated profusely with excellent plates, and is well indexed. The style of the writer, as is usual with British authors, is faultless. The book is full of stimulus and suggestion, and represents many years of careful observation and hard work.

H. B. S.

The Stomach, Intestines and Pancreas. By W. C. Bosanquet, M. D., and H. S. Clogg, M. S. Edited by James Cantlie, M. B. (*New York: William Wood & Co., 1912.*)

In this work we have an attempt to discuss the diseases concerned from both the medical and surgical aspects. Such an effort in the scope of a small volume can only hope to be successful in so far as is permitted by the limitations of space. The authors on the whole have succeeded in giving a clear summary of the subject. There are two questions connected with disease of the intestinal tract on which opinion is as widely different on the two sides of the Atlantic as they are apart geographically. These are mucous colitis and appendicitis. The essential point in the etiology of mucous colitis which is most important for proper treatment is the recognition of the fact that it is nearly always secondary to a general nervous disturbance. Unless this can be remedied the local condition is not permanently benefited. Yet in the discussion of treatment in this work no reference is made to this fact and it is small wonder that the authors speak of treatment as being unsatisfactory. Of course it is if the cause is not recognized and remedied. The treatment of appendicitis as given here is most unsatisfactory. To give as the indication for operation in ordinary acute appendicitis the recognition of a spreading peritonitis deserves strong condemnation. It would be interesting to ask the authors how often they have regretted operating too early and how often too late in an acute case. It is quite correct as they say that "the majority of cases of appendicitis will subside," but what about the minority which will not subside and in which delay often means death? In most diseases the *majority* recover; our fight is to save some of the minority.

Despite these points which deserve criticism, there is much in the work to be commended, its limitations always being recognized.

Augustus Charles Bernays. A Memoir. By Thekla Bernays. $2. (*St. Louis: C. V. Mosby Company, 1912.*)

Those who only knew Bernays as a brilliant surgeon will be glad to read this account of him by his sister and learn the kind of man he was. The memoir is frank and does not conceal the man's failings—this is as Bernays would have had it, for he was fearless, frank, and indifferent to the common judgment of men. He was never married and for many years lived and traveled much with his sister. Born of German parents he had all the characteristic German family feeling and was devoted to her, who, equally devoted to him, has written a brief story of his life. Allowing for the natural overflow of a sister's feelings for her brother, who was so fine a surgeon, and had so much kindliness of heart, this memoir portrays him vividly, and the reader is left with an empression of a man big in many ways.

Methods of Organic Analysis. By Henry C. Sherman, Ph. D. Second edition, rewritten and enlarged. $2.40. (*New York: The Macmillan Company, 1912.*)

The first edition of this work was favorably commented upon in our columns (May, 1906), and the new edition demands also a word of praise. The author in enlarging his original work has done so with skill, so that its use as a text-book is unimpaired in this respect, and the new chapters add important material for students, to whom the work can be warmly commended.

Clinical Disorders of the Heart Beat. A Handbook for Practitioners and Students. By Thomas Lewis, M. D. $2. (*London: Shaw and Sons; New York: Paul B. Hoeber, 1912.*)

The purpose of this little book is to acquaint the general practitioner with the essential facts which researches by means of graphic methods in the study of the heart-beat have contributed to the practice of medicine and to enable him to make practical use of these data without having to resort to the more elaborate methods of diagnosis.

The book opens with an introductory chapter upon the general characteristics of the principal types of cardiac disorder encountered clinically: Sinus arrhythmia, heart-block, premature contractions, paroxysmal tachycardia, auricular fibrillation, alternation of the pulse. The subsequent chapters are devoted to a concise discussion of the main clinical characteristics, diagnosis, prognosis and treatment of each of these forms. No attempt is

made to give references or the names of investigators in the subject. Etiological factors encountered by the author in a large series of his own cases are given in tabular form, and the course of the abnormal impulses within the heart is indicated by very simple diagrams.

In the clinical diagnosis of arrhythmias, the author calls attention to the characteristics of the heart sounds and radial pulse, by which fairly accurate functional diagnoses may be made in a considerable number of cases. Inspection of the pulsation over the jugular veins, however, does not receive adequate attention, although by this simple method, in the reviewer's experience, the practitioner's accuracy and refinement of diagnosis may be greatly increased.

The discussion of heart-block is in the main excellent. One statement of the author is worthy of comment. He writes that the milder forms of heart-block "often require digitalis medication, and this will frequently increase the grade of block. But the increase of block should not deter digitalis administration for the relief of dilatation, dropsy or other symptoms, nor is it in itself detrimental, the drug or its allies may be given without restraint and often beneficially." This is in direct contrast to the almost universal clinical experience and the experiments of v. Tabora which indicate administration of digitalis in cases of *partial* heart-block often suddenly cuts off all conduction and precipitates attacks of syncope before the cumulative action of the drug can affect the ventricular muscle sufficiently to increase its automaticity. The experience of most observers is that the use of digitalis is almost always contraindicated in partial block and indicated after complete block has once become established. As might be expected from the experimental work of the writer, the subject of auricular fibrillation is particularly well discussed in all its phases.

The style of the book is clear, direct and fluent, and the book may be commended to the general practitioner who desires a small monograph upon this phase of the subject.

A. D. Hirschfelder.

The Theory of Schizophrenic Negativism. By Professor E. Bleuler. Translated by Wiliam A. White, M. D. 60 cts. (*New York: The Journal of Nervous and Mental Disease Publishing Company, 1912.*)

Dr. White, the Superintendent of the Government Hospital for the Insane, Washington, D. C., who has himself contributed two noteworthy monographs to this series published by The Journal of Nervous and Mental Disease, again puts the profession under obligation to him by this skilful translation of Dr. Bleuler's brief paper. Psychiatrists who do not read German fluently will be especially grateful for the publication of this important article to which we are glad to call attention.

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Compendium of Diseases of the Skin. Based on an Analysis of of Thirty Thousand Consecutive Cases with a Therapeutic Formulary. By L. Duncan Bulkley, A. M., M. D. Fifth revised edition of the Manual of Diseases of the Skin. 1912. 8vo. 286 pages. Paul B. Hoeber, New York.

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A Manual of Clinical Chemistry, Microscopy, and Bacteriology. By Dr. M. Klopstock and Dr. A. Kowarsky. Only authorized translation from the last German edition, thoroughly revised and enlarged. Illustrated with forty-three textual figures and sixteen colored plates. [1912.] 12 mo. 371 pages. Rebman Company, New York.

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THE DETERMINATION OF THE EQUILIBRIUM IN THE HUMAN BODY BETWEEN ACIDS AND BASES WITH ESPECIAL REFERENCE TO ACIDOSIS AND NEPHROPATHIES.*

By Andrew Watson Sellards,
Assistant Resident Physician, The Johns Hopkins Hospital.

OUTLINE.

I. Maintenance of Normal Equilibrium:
  1. By food supply;
  2. By elimination (especially from the kidneys and lungs);
  3. By the formation of ammonia from protein.
II. Maintenance of Equilibrium in Conditions of Acidosis:
  1. By utilization of the reserve supply of fixed bases of the tissues;
  2. By increased elimination;
  3. By the increased formation of ammonia.
III. General Method for Detecting Disturbances of this Equilibrium by the Determination of the Tolerance of the Body to Bases:
  1. In normal individuals;
  2. In acidosis;
  3. In unknown conditions.
IV. Summary:
  1. Behavior in diabetes;
  2. Interpretation of ammonia coefficient;
  3. Behavior in various nephropathies.

In order to meet the changing conditions of our environment and to control the series of alterations which are continually taking place within the body, we find that a normal equilibrium, in many instances, is maintained by means of balanced mechanisms. These mechanisms affect various systems of the body and they involve both physical and chemical reactions. Some of the better known examples are the heat regulating mechanism and the balance between water and salts to maintain a normal osmotic pressure. It will also be remembered that many diverse chemical processes taking place within the body are closely dependent upon a delicate adjustment of the reaction of their medium and it is found that the concentration of acids and bases in the body fluids remains comparatively constant in the presence of many normal and pathologic factors which tend to disturb this equilibrium. The compensation which is maintained is sufficiently effective, except in extreme conditions, to prevent any pronounced change in the reaction of the body fluids even though extensive metabolic changes may be taking place within the body. Thus a very considerable increase in the acid end-products of metabolism may be accompanied by only a slight change in the values obtained by titration for the acidity of the urine and the alkalinity of the blood. Therefore, other methods, in addition to the examination of the body fluids, must be used to detect the full extent of the changes which are taking place in the body and it is the purpose of this paper to consider such methods.

General Considerations.

Normal Equilibrium.—Under normal conditions, upon a mixed diet, there is a continuous interchange in the body between acids and bases. The food supply yields a limited

* From the Chemical Division of the Medical Clinic.

amount of bases, but the acid forming substances usually predominate, the proteins yielding considerable acid on account of their content in sulphur and phosphorus. Two important methods suffice to compensate for the excess of acids over bases that ordinarily occurs in a mixed diet. The adjustment of the smaller variations appears to be very effectually controlled by the kidney; either acid or base is promptly excreted, according as one or the other is present in excess in the blood stream. Thus, although the reaction of the blood is constantly alkaline, the kidney in the formation of urine, is able to separate the acids from their combinations with the bases, excreting acid salts and retaining the bases, in part at least, in the blood. This function of the kidney apparently represents one of the important activities of this organ, but the exact process is but little understood.

Ordinarily there is a constant excretion of moderate quantities of ammonium salts in the urine, and this is usually interpreted as indicating that a slight grade of acidosis exists even under normal conditions. One objection which has been advanced against this view is that traces of ammonia continue to appear in the urine even though its reaction is kept constantly alkaline by the administration of carbonates. Furthermore the quantities of sodium bicarbonate which are required to reduce materially the normal output of ammonia are considerably in excess of the calculated values. An examination of the data recently reported by Janney[1] illustrates this characteristic. Perhaps these two features may be explained on a common basis. But whatever their explanation may be, the consensus of opinion is that practically all of the ammonia which appears normally in the urine has been intercepted in the course of urea formation for the neutralization of acids.

Pathologic Conditions.—The means by which the body compensates for pathologic excesses of acid consist essentially in a quantitative increase in the normal processes of metabolism. The principal compensatory changes are as follows:

I. Increased output in the urine of:
   1. Acid radicals,
   2. Fixed bases, and
   3. Ammonia nitrogen.

In severe grades of acidosis this results in:

II. Decreased content of the blood in:
   1. Fixed bases, and
   2. Carbon dioxide.

These quantitative changes represent general non-specific alterations resulting from the increased accumulation of hydrogen ions. Theoretically, such changes should occur in any acidosis independently of the nature of the acid in question.

The qualitative changes, on the other hand, depend upon the ætiologic factor and are represented, as a rule, by the appearance of a foreign acid; in starvation acidoses, these changes are absolutely qualitative since β-oxybutyric and acetoacetic acid are not found under normal conditions. Likewise, the appearance of acetone from the oxidation of these acids constitutes a change which, for practical purposes, is essentially qualitative in character.

[1] Janney: Ztschr. f. physiol. Chemie, Strassb., 1912, LXVII, 99.

Methods of General Application.

These qualitative and quantitative changes constitute evidence of the disturbance of equilibrium in the content of the body in acid and base. The behavior of acetone and acetoacetic and β-oxybutyric acid has been studied with especial care in the starvation acidoses and the tests for these substances are particularly applicable for the detection of such conditions. However, in the development of the theory of acidosis, it would seem desirable to possess a method which would not be limited to any one acid, but would be of general application.

A consideration of the quantitative changes occurring in acidosis shows that many of them would not afford a suitable basis for the development of a general method. The detection of the increased output of fixed bases in the urine is not particularly feasible as a routine procedure. Moreover, the kidney is able to increase the excretion of acid radicals only to a very limited extent above the normal. Likewise the compensatory processes of the body are usually sufficient to prevent any striking diminution in the alkalinity of the blood.

The carbon dioxide content of the blood may show extreme diminution, but apparently this change takes place only in the very advanced stages of acidosis.

Without question, one of the most important sources of bases consists in the formation of ammonia from protein, and the increase in its excretion offers valuable evidence in the detection of acidosis. Theoretically, one would expect an increase in the production of the ammonium salts in any acidosis. However, in the interpretation of the ammonia metabolism there are two considerations which are of primary importance. In the first place one would require to know the sensitiveness with which the body responds by an increase in ammonia production; for when the output is normal, one could exclude the possibility of the presence of an early stage of acidosis only if it were known that a slight increase in acid is accompanied by an increase in ammonia. On the other hand, in making a positive diagnosis on the basis of a high ammonia nitrogen, it is necessary to exclude a primary disturbance of protein metabolism resulting in an increased output of ammonia. Cases illustrating these conditions will be discussed later. In general, it may be said that any signs indicating an hepatic lesion would complicate the interpretation of the ammonia metabolism. Even in diabetes the nitrogen partition in the urine does not always behave merely as a secondary disturbance of metabolism. Thus if the increase in ammonia were a purely compensatory process, it should cease when a liberal supply of base is provided. However, especially among advanced cases, instances not infrequently occur in which this increase continues in the presence of an abundance of carbonates.[2] Under certain

[2] von Noorden considers that a primary disturbance of protein metabolism may occur in diabetes. His evidence is based on an increase in the output of purin nitrogen.

conditions, therefore, it may be difficult to determine whether an increased ammonia coefficient represents a purely compensatory process or whether it also involves a primary disturbance in the nitrogen metabolism.

On theoretical grounds it would seem that the behavior of the body toward the fixed bases would supplement the conclusions derived from the data concerning the production of ammonia. We have, therefore, two procedures which apparently would be applicable in any acidosis, namely, (1) the study of the ammonia excretion, and (2) the fate of the fixed bases upon introduction into the body. As regards the relationship between these methods, the features which present themselves more prominently for consideration are the relative sensitiveness of these two procedures and the effect of various complicating factors upon the interpretation of the results which they yield. Accordingly, I have undertaken the study of the effect of the administration of bases with a view to the development of a method for determining the state of equilibrium in the body between acids and bases. This has been undertaken, not so much from a chemical or physico-chemical point of view, but rather by the use of methods which involve physiological reactions.

Ordinarily, the body conserves its supply of base with considerable care. Thus in the lungs the carbon dioxide is liberated from the acid carbonates and is excreted as such; in the kidneys the acid radicals, which have been neutralized by bases, are again converted into acid salts. In both instances the bases, in part at least, are retained in the body. The method which was adopted to establish the normal conditions of equilibrium consisted in the determination of the quantity of base which it is necessary to introduce into the body in order to bring about its excretion in the urine. Of the many procedures which might be suggested this one has afforded a satisfactory basis for determining the point at which the body contains an excess of bases. An increase beyond the normal in the amount of base which the body can take up might represent, therefore, an increase in the production of acid. On the other hand, the spontaneous excretion of bases does not ordinarily occur in sufficient quantity to indicate a pathologic disturbance.

Determination of Tolerance to Fixed Bases.

In adopting a routine for the determination of the behavior of individuals toward bases under normal and pathologic conditions, the following questions have been considered:

1. Choice of base;
2. Method of administration, and
3. Collection and examination of urine specimens.

In the selection of a suitable base one may consider either the hydroxides themselves or some of the substances which readily give rise to hydroxyl ions upon solution in water, such as the salts of the weak acids, especially carbonic acid. Sodium bicarbonate was chosen in preference to the normal carbonate, sesqui-carbonate, or the hydroxide. Although the carbonate may, perhaps, be more suitable in the therapy of advanced stages of acidosis, yet for diagnostic purposes, where the acidosis may be slight in extent or absent, the bicarbonate seems preferable in order to avoid the caustic properties of the normal carbonate. One might even employ the neutral salts of the organic acids (*e. g.*, sodium acetate) depending upon their oxidation to carbonates, but any involvement of the oxidative processes of the body would introduce complicating factors.

As a general rule, except when large quantities were to be used, a 2 per cent solution of sodium bicarbonate was employed. The following precautions were adopted in order to avoid too extensive loss of carbon dioxide with conversion of the bicarbonate into the carbonate. Sterilization was carried on at a pressure of 10 lbs. for 30 minutes in an atmosphere of carbon dioxide. This was generated by placing a moderate quantity of sodium bicarbonate in the water supplying the autoclave. The sterilizer was always cooled to room temperature before opening. Ordinary cork stoppered bottles were used as containers for the 2 per cent solution. It was found that these bottles could be fairly effectively closed during sterilization by tying the cork stoppers in place. The solutions were kept securely stoppered and were used not later than two or three days after sterilization. Under these conditions sterilization could be readily effected without converting more than 5 to 10 per cent of the bicarbonate into carbonate. This amount of change is not greater than occurs at ordinary temperatures when bicarbonate is dissolved in water. Throughout this paper the term bicarbonate is used to apply to both the salt itself and its solutions, though in the latter a certain proportion of the bicarbonate gives rise to carbonate and hydroxyl ions.

As regards the method of administration, it is desirable that the sodium bicarbonate may be given either by the mouth or by intravenous injection, in order that one may have a choice of procedure according to the individual case under consideration. Thus in some of the cardio-vascular conditions there are complications in which intravenous injections are not suitable. Also, instances may frequently occur in which intravenous injections are unnecessary, inasmuch as the ingestion tests suffice to show that normal conditions exist. The principal disadvantage of ingestion of bicarbonate depends upon the question of assimilation. There would appear to be no reasonable doubt about the assimilation when small amounts are administered and when the condition of the gastro-intestinal tract is normal. This, however, introduces rather important limitations in the quantities which can be employed.

Injection methods are essential if large amounts are to be given or if conditions such as nausea, pyloric obstruction, or diarrhœa exist. By inserting the injection needle directly into the vein without incising the skin, one can introduce comparatively large quantities with a minimal amount of discomfort to the patient.

In the examination of the urine I have used only very simple methods. Quantitative estimations of the amount of carbonates recovered in the urine were not attempted. The rather wide variation in the behavior of the urine toward the various indicators complicates the direct application of titration methods for the determination of alkalinity, and it would seem that no suitable applications of the alkalimetric processes have been developed for the examination of urine. Only qualitative

tests have been employed. With litmus as an indicator it was assumed that, if the urine is definitely acid, there can be no carbonate or bicarbonate present. One point, however, is essential, namely, that specimens which are only slightly acid should be thoroughly boiled, since the bicarbonate may be excreted as such and it reacts less readily with litmus than normal carbonate. Thus, it frequently happens that a specimen of urine which is neutral or slightly acid to litmus will become slightly alkaline on boiling. None of the conditions have arisen in which a slightly alkaline urine becomes acid on boiling except where ammoniacal fermentation has occurred. The duration of the persistence of the alkaline reaction has also been noted.

An exact regulation of some of the minor conditions which affect the reaction of the urine was not attempted inasmuch as it seems preferable to establish a normal standard which at least would be beyond the influence of such factors as the ordinary variations in diet and in water intake. Under certain circumstances the frequency of micturition might influence the reaction. In some of the conditions which have been studied, particularly in uræmia, it is impossible to obtain specimens of urine at any fixed intervals. The one precaution which was observed in pathologic conditions was to obtain urine specimens, when possible, as often as every three or four hours and in all instances to avoid the accumulation in the bladder of excessively large amounts of urine. In a portion of the work a uniform period was adopted, specimens being collected every three hours.

Normal Individuals.—The determinations which have been reported [3] of the tolerance of normal individuals to intravenous injection show that, at least under certain conditions, small amounts of sodium bicarbonate will effect a change in the reaction of the urine. Thus, in eight cases, four individuals received quantities of 4½ to 5 grams and responded promptly with an alkaline urine. In four other cases, receiving smaller amounts, namely, 2 to 3 grams, the results varied: in two of these individuals the urine became alkaline, but in the other two it remained acid.

In order to extend these data an additional series of cases has been tested with the purpose of determining the efficiency of ingestion methods. In the selection of individuals, normal adult males were chosen. These men were living on an ordinary mixed diet and, for the most part, they were taking but little exercise. While this represents the standard conditions under which one would expect to carry out tests on pathologic cases, yet in the interpretation of data it would be more satisfactory to know the maximum quantities of sodium bicarbonate that would be just sufficient to bring about an alkaline reaction of the urine under any conditions that could be regarded as essentially normal. Perhaps the highest quantities might be required in men who are performing heavy labor and taking an abundant meat diet. While we have no data for this class, still some evidence has been obtained which has some bearing on the maximum values that might be expected. Since under normal conditions certain individuals may excrete an alkaline urine, it has seemed sufficient for the present purposes to determine only the maximum values that may be required.

The question of the proportion between the weight of the individual and the dosage of bicarbonate is not a simple one. If an increase in weight involved a proportional increase in each of the important constitutents of the body, more especially the water, protein and fat, then calculations of dosage per kilo of body weight would be desirable. However, if the increased weight of an individual under consideration is due to an increase, for example, of fat alone, then the comparison of individuals might be more accurate than the regulation of the dosage in proportion to the body weight. Accordingly, in the absence of an exact basis on which to proceed, constant quantities of bicarbonate have been used and the weight of the individual has been recorded.

The first group of cases in Table I gives the preliminary results, showing the effect of the ingestion of 5 grams of sodium bicarbonate. Only those individuals were tested whose urine was distinctly acid to litmus. Specimens of urine were not collected at fixed intervals. In some instances several repetitions of the test were made in the same individual.

TABLE I.

SHOWING THE EFFECT OF THE INGESTION OF 5 GRAMS OF SODIUM BICARBONATE ON THE REACTION OF THE URINE IN NORMAL INDIVIDUALS.

Individual.	Interval between tests.	Weight (lbs.).	Reaction of urine before ingestion of bicarbonate.	Interval between specimens (hrs.).	Reaction to litmus.	Interval between specimens (hrs.).	Reaction to litmus.	Interval between specimens (hrs.).	Reaction to litmus.	Interval between specimens (hrs.).	Reaction to litmus.	Duration of change in reaction (hrs.).
A	....	180	Ac.	4½	Alk.	3½	Ac.	..	....	..	....	4½
	2 days	..	Ac.	4½	Amphot.	3	Amphot.	3	Ac.	..	....	7½
	7 days	..	Ac.	2	Alk.	7½	Ac.	..	....	..	....	2
	6 wks.	..	Ac.	3	Alk.	6	Alk.	2	Ac.	..	....	9
B	....	130	Ac.	2	Alk.	2	Ac.	2	Alk.	1½	*Neut.	..
	3 days	..	Ac.	4	Ac.	2	Ac.	2	Alk.	1½	Ac.	2
	4 days	..	Ac.	2	Alk.	2	Alk.	3	Ac.	..	....	4
	25 days	..	Ac.	3	Alk.	3	Ac.	2	Amphot.	3	Ac.	3
C	....	130	Ac.	3	Alk.	3	Ac.	..	....	..	...	3
	7 days	..	Ac.	3	Alk.	3	Ac.	..	....	..	....	3
D	....	125	Ac.	2½	Ac.	3½	Amphot.	3½	Neut.	2	*Neut.	9
E	....	150	Ac.	3½	Alk.	3	Alk.	2	Alk.	2	Ac.	8½
F	....	155	Ac.	Alk. for 10 hrs.			....	..	....	..	....	10

* The succeeding specimen was acid.

In an additional group the ammonia coefficient was determined and the degree of acidity of the urine was estimated in order to insure the selection of some cases in which the acid metabolism approached the maximum values which occur under normal conditions. In this group the urine was collected, as far as possible, at intervals of three hours.

[3] Sellards: Philippine J. Sc., B. Manila, 1910, V, 363; Sellards and Shaklee: Ibid., 1911, VI, 53.

TABLE I—Continued.

Individual.	Weight (lbs.).	Character of urine before administration of bicarbonate.			Sodium bicarbonate, grams.	Reaction of urine after bicarbonate.		Repetition of sodium bicarbonate, grams.†	Reaction of urine after bicarbonate.		Duration of change in reaction.
		Litmus.	Acidity.*	Ammonia coefficient.		3 hours.	6 hours.		9 hours.‡	12 hours.‡	
A	180	Ac.	6.0	4.4%	5	Alk.	Alk.	0	Ac.	Ac.	6
B	130	Ac.	3.7	4.1%	5	Alk.	Ac.	0	....	....	3
D	125	Ac.	3.0	3.8%	5	Ac.	Alk.	0	Alk.	Ac.	6
F	155	Ac.	1.2	5.9%	5	Ac.	Alk.	0	Ac.	....	3
G	135	Ac.	3.5	5.1%	5	§ Very faintly ac.	Ac.	0	Ac.	Ac.	..
‖G	...	Ac.	3.5	4.4%	5	Alk.	Ac.	0	Ac.	Ac.	3
H	110	Ac.	3.6	4.4%	5	Alk.	Ac.	0	Ac.	Ac.	3
I	140	Ac.	2.8	4.0%	5	Ac.	Ac.	5	Alk.	18 hrs.	18
J	150	Ac.	3.3	5.3%	5	Ac.	Ac.	5	Alk.	Ac.	3

* Per cent of N/1 solution (titrated with phenolphthalein).
† Six hours after the first administration.
‡ That is, after the first administration of bicarbonate.
§ Well-marked precipitate of phosphates on boiling.
‖ Repetition after 5-day interval.

Certain minor differences were noted in regard to the manner in which the various cases reacted. In many instances the reaction changed suddenly from acid to alkaline and then returned promptly to a definitely acid reaction. In others the change was much slower, the reaction gradually becoming neutral or slightly alkaline, and then returning first to a faintly acid, and eventually to a distinctly acid reaction. In one instance (Individual B) there was a distinct tendency, after the administration of bicarbonate, for the urine to fluctuate between a faintly acid and a faintly alkaline reaction. This case, however, constituted an exception, the rule being that the acid reaction would persist after it had once returned.

Another point which is of especial importance in connection with the testing of pathologic cases is the interval of time which is required for the bicarbonate to take effect. In the series of intravenous tests, which were referred to, the alkaline reaction frequently made its appearance at an early period, sometimes within one hour after injection. In the preceding ingestion tests an alkaline reaction often appeared after an interval of three hours. In subsequent work with cases which showed an increase in tolerance, it was considered permissible to repeat the bicarbonate after an interval of six hours and in some instances small doses were repeated at intervals of three hours. This increases the danger of exceeding the minimal quantity which might be required, but this can be partially controlled by observing the length of time that the alkaline reaction persists.

From the data in Table I it is seen that although the ingestion of 5 grams of sodium bicarbonate in one dose was not always sufficient to bring about an alkaline reaction of the urine, yet it usually produced a definite and readily appreciable effect, the reaction changing, for instance, from a distinctly acid to a neutral or faintly acid reaction with precipitation of phosphates on boiling. The two cases in which no effect was produced were neurotic men who were taking limited amounts of fluid and were excreting small quantities of urine, the rate being as low as 25 cc. for periods of three hours. After an interval of six hours the 5 gram quantity was repeated and both individuals responded promptly with an alkaline urine.

After considering the preceding data it seemed desirable to determine whether or not one might find any individuals who would fail to excrete bicarbonate in the urine after the ingestion of 10 grams at one dose. This amount is so much in excess of the quantity which is required in the majority of instances that it would seem best to select individuals who would probably require larger amounts than are ordinarily necessary. Instead of looking for cases in which the acid metabolism had spontaneously reached the upper limits of normal, it seemed feasible to produce a slight increase in the normal degree of acidosis. The data in the following outline are compiled from subsequent tables showing the behavior of individuals toward 10 grams of sodium bicarbonate after two days of carbohydrate free diet.

Ingestion of 10 Grams of Sodium Bicarbonate After Two Days of Carbohydrate Free Diet.

Reaction of urine.	Total acetone (grams per day).	β-oxybutyric acid (grams per day).	Effect on the reaction of the urine.
Ac.	0.692	2.374	Amphot. 9 hrs.
Ac.	0.282	0.184	Amphot. 3 hrs.
Ac.	0.621	1.111	Neut. 3 hrs.

In all of these cases a distinct effect was produced upon the reaction of the urine. It would seem a little unexpected if spontaneous fluctuations in diet could produce as much change as that resulting from two days of carbohydrate free diet.

Tolerance to Sodium Bicarbonate in Acidosis.

The next step which was undertaken was the study of the behavior of the body in a state of acidosis to the introduction of sodium bicarbonate. In order to compare this behavior with the usual signs of acidosis it seemed desirable to work with acidoses produced artificially rather than those occurring spontaneously. For purposes of study the production of an artificial acidosis possesses several advantages. The exact cause of the acidosis and the degree to which it extends is under control. Furthermore, before the production of the acidosis, one can determine the normal condition of the individual under consideration.

It might appear *a priori* that the introduction of bicarbonate into the body would serve for the detection of acidosis only in comparatively advanced conditions. In considering the degree of delicacy which one might expect from such a procedure it may be well to consider the usual course of events in an acidosis. It is generally accepted that, even in the terminal stages of diabetic acidosis, no free acid exists in the fluids of the body which are in general circulation, *i. e.*, the acid produced in the tissues has not only been neutralized, but,

at least, a slight excess of base predominates and the blood retains an alkaline reaction. Consequently, upon the introduction of bases into the body, the hydroxyl ions do not meet with free hydrogen ions and instead of neutralizing acids immediately the bases are taken up by the tissues in order to replace those which have been previously removed by acid.

It would seem, therefore, that the delicacy of the method in question would depend essentially, in the first place, upon the promptness with which the tissues give up their fixed bases when the acid metabolism increases, and secondly upon their capacity for binding sodium bicarbonate when it is presented to them. One important question which suggests itself is whether the introduction of comparatively large amounts of bicarbonate, either directly into the blood stream or through the alimentary tract, might not result in a temporary overwhelming of the kidney with bicarbonate, resulting in its excretion in the urine before the tissues could make good any deficiency which they might have suffered.

Routine.—For the production of acidosis, carbohydrate starvation was used as the principal method, though some preliminary tests were carried out in which mineral acid was introduced into the body without any alteration in the diet.

The signs of acidosis which were observed in the starvation cases were as follows:

1. Titration of the degree of acidity of the urine by Folin's[4] method.
2. Estimation of the total acetone and the β-oxybutyric acid by Shaffer's[5] method. (The total acetone includes both the preformed acetone and the acetoacetic acid.)
3. Determination of the ammonia coefficient.
4. Determination of the tolerance to sodium bicarbonate.

Analyses of the blood for alkalinity or carbon dioxide content were not made, inasmuch as no well-developed grades of acidosis were produced.

These tests were first carried out while the individual was on an ordinary mixed diet. Then a carbohydrate free diet was maintained, usually for a period of two days, and on the third day the tests were repeated, the carbohydrate free diet being maintained until the completion of the tests. Ordinarily the determination of the tolerance to sodium bicarbonate did not occupy an entire day. In Table II the figures given in parenthesis for the final day of each test represent the calculated values for a 24-hour period; these calculations are based on the data obtained for the fraction of the 24 hours during which the observations were made. On account of the necessity of introducing this calculation, the quantities per liter have been recorded as well as the quantities per day.

After a few determinations it was found that the response to the carbohydrate free diet, in most instances, was not sufficiently great to effect an increase in the ammonia coefficient. The general behavior of the ammonia coefficient is recorded in the first two cases in Table II (A and D). In the majority of the remainder of the cases the degree of acidosis did not appear to be sufficient to warrant the determination of the ammonia nitrogen. The titration of the degree of acidity of the urine did not show significant changes except in one instance, where the acidity was unusually low at the beginning of the period of carbohydrate free diet. These data were not of sufficient interest to be included in the tables.

In all instances the sodium bicarbonate was given by ingestion. One important point on which information was desired was the manner of estimating the dosage of bicarbonate in unknown conditions. In those cases in which there is no guide concerning the quantity which will be required, the most feasible procedure consists in starting with an amount which can be readily borne by a normal individual. This quantity may then be repeated or even increased according to the behavior of the individual in question. The behavior of the normal individuals recorded in Table I was taken as a guide in determining the interval of time at which a repetition should be made. The maximum interval which has been used in the ingestion tests is six hours. In some instances an interval of three hours has been used and this seems to involve comparatively little danger in overstepping the amount of bicarbonate which is required.

In addition to the carbohydrate starvation cases, some preliminary observations were made on the effect of the ingestion of mineral acids. In two cases dilute hydrochloric acid was used in quantities of 2 cc. three times per day for four and five days. The absolute quantities for the total period were

TABLE II.

Showing the Tolerance to Sodium Bicarbonate After One to Three Days of Carbohydrate Free Diet, Tested by the Ingestion of 5 Grams of Sodium Bicarbonate Every Six Hours.

Individual.	Day.	Diet.	Ammonia coefficient.	Total acetone (grams).		β-oxybutyric acid (grams).		Tolerance to sodium bicarbonate.	
				Per liter.	Per day.	Per liter.	Per day.	Gms.	Effect on urine.
A	1	Mixed.	2.7	0.010	0.015	0.057	0.084		
	2	Do.	2.2	0.010	0.014	0.067	0.094	5	Alk. 6 hrs.
	3	Do.	2.5	0.012	0.010	0.110	0.090	..	
	4	Do.	3.1	0.017	0.015	0.081	0.073	..	
	5	Carbohydrate free.	3.3	0.144	0.106	0.139	0.103	..	
	6	Do.	*1.9	0.329	(0.230)	0.249	(0.174)	10	Alk. 3 hrs.
D	1	Mixed.	....	.....	.....	.....	.....	5	Alk. 3 hrs. Neut. 3 hrs.
	2	Do.	3.8	0.010	0.011	0.053	0.062	..	
	3	Carbohydrate free.	2.7	0.018	0.027	0.086	0.127	..	
	4	Do.	2.4	0.230	0.161	0.381	0.267		
	5	Do.	*1.9	0.758	0.856	1.705	1.927	25	Alk. 6 hrs.
G	1	Mixed.	....	.....	.....	.....	.....	5	Faintly ac.
	2	Carbohydrate free.	....	0.027	0.054	0.00	0.00	..	
	3	Do.	....	0.031	0.036	0.080	0.092		
	4	Do.	....	0.028	(0.049)	0.054	(0.094)	15	Alk. 6 hrs.
H	1	Mixed.	....	.....	.....	.....	.....	5	Alk. 12 hrs.
	2	Carbohydrate free.	....	0.032	0.035	0.035	0.038	..	
	3	Do.	....	0.083	0.079	0.130	0.123	..	Neut. 3 hrs.
	4	Do.	....	0.188	(0.263)	0.142	(0.200)	5	Alk. 3 hrs.
K	1	Mixed.	....	.....	.....	.....	.....	5	Alk. 3 hrs.
	2	Carbohydrate free.	....	0.023	0.040	0.042	0.074	..	
	3	Do.	....	0.045	0.074	0.071	0.116	..	Alk. 9 hrs.
	4	Do.	....	0.160	0.272	0.170	0.289	20	Amphot. 3 hrs

* During the administration of bicarbonate.

[4] Folin: Am. J. Physiol., Bost., 1903, IX, 265.

[5] Shaffer: J. Biol. Chem., Balt., 1908, V, 211.

TABLE II—Continued.

Showing Tolerance to Sodium Bicarbonate on the Third Day of Carbohydrate Free Diet.

(1) INGESTION OF 10 GRAMS SODIUM BICARBONATE IN ONE QUANTITY.

Individual.	Day.	Diet.	Total acetone (grams).		β-oxybutyric acid (grams).		Tolerance to sodium bicarbonate.	
			Per liter.	Per day.	Per liter.	Per day.	Gms.	Effect on urine.
F	1	Mixed.	.....	.....	.....	.....	5	Alk. 12 hrs.
	2	Carbohydrate free.	0.011	0.010	0.036	0.032	..	
	3	Do.	0.015	0.025	0.038	0.065	..	
	4	Do.	0.322	(0.692)	1.104	(2.374)	10	Amphot. 9 hrs.
H	1	Mixed.	.....	.....	.....	.....	5	Alk. 3 hrs.
	2	Carbohydrate free.	0.032	0.035	0.035	0.038	..	
	3	Do.	0.083	0.079	0.130	0.123	..	
	4	Do.	0.188	(0.282)	0.142	(0.184)	10	Amphot. 3 hrs.
L	1	Mixed.	.....	.....	.....	.....	5	Alk. 3 hrs.
	2	Carbohydrate free.	0.363	0.254	0.634	0.444	..	
	3	Do.	0.298	0.620	0.363	0.755	..	
	4	Do.	0.414	(0.621)	0.741	(1.111)	10	Neut. 3 hrs.
(2) INGESTION OF 5 GRAMS SODIUM BICARBONATE EVERY 3 HRS.								
I	1	Mixed.	.....	.....	.....	.....	*10	Alk. 18 hrs.
	2	Carbohydrate free.	0.054	0.054	0.073	0.073	..	
	3	Do.	0.077	0.069	0.240	0.216	..	
	4	Do.	0.255	(0.255)	0.313	(0.313)	10	Very faintly ac. 6 hrs.
J	1	Mixed.	.....	.....	.....	.....	*10	Alk. 3 hrs.
	2	Carbohydrate free.	0.048	0.082	0.087	0.148	..	
	3	Do.	0.064	0.109	0.139	0.236	..	
	4	Do.	0.170	(0.289)	0.257	(0.437)	15	Very faintly ac. 6 hrs.

* Two quantities of 5 grams at intervals of 6 hours.

2.8 and 2.2 grams. As will be seen in the accompanying outline, the rise in tolerance to sodium bicarbonate was perhaps even slightly greater than could be accounted for by the bases which this amount of acid could withdraw, 2.8 grams hydrochloric acid corresponding to 6½ grams, and 2.2 grams to 5 grams of sodium bicarbonate. In the third case about half of this quantity of acid was used and, as would be expected theoretically, no rise in tolerance occurred.

TABLE III.

Showing the Tolerance to Sodium Bicarbonate After the Ingestion of Hydrochloric Acid.

Individual.	Day.	Acidity of urine.*	Ammonia coefficient.	Ingestion of hydrochloric acid.	Tolerance to sodium bicarbonate.†	
					Gms.	Effect on reaction of urine.
L	1	1.4	5.9	None.	5	Alk. 6 hrs.
	7	2.3	5.8	2.8 grams in 5 days.	‡15	Reaction reduced to slightly acid for 3 hrs.
M	1	1.5	5.0	None.	5	Alk. 3 hrs.
	6	2.6	5.4	2.2 grams in 4 days.	‡15	Alk. 3 hrs.
N	1	...	...	None.	5	Alk. 3 hrs.
	6	...	...	1.2 grams in 4 days.	10	Alk. 15 hrs.

* Per cent N/1 solution (titrated against phenolphthalein).
† Second test was made 15 hours after the last administration of hydrochloric acid.
‡ 10 grams at the first dose and 5 grams 6 hours later.

This series was not extended any further inasmuch as the ingestion of hydrochloric acid is not very well borne and these controls are not altogether essential.

The data for the tolerance tests in Table II would, in many instances, be without significance except for the fact that the normal, for the individual under consideration, had been determined only a few days before. Under these circumstances the conclusion would seem to be justified that the tolerance to sodium bicarbonate begins to rise very early in the course of an acidosis. This would indicate that an increased production of acid was met in part by the fixed bases of the tissues and not wholly by an interception of ammonia and by the excretion of acid salts. Observations which are related to these data have been made upon the ammonia excretion and the acidity of the urine after the ingestion of food containing an excess of acid forming elements. After the ingestion of the equivalent of as much as 32.7 cc. normal acid per day, Sherman and Gettler[6] found that the increase in the output of ammonia and acid salts in the urine was sufficient to account for only about three-fourths of the ingested acid. However, they do not attribute the neutralization of the remainder to the fixed bases.

Of the three procedures used in Table II for the administration of the bicarbonate, it would seem that the ingestion of 5 grams every six hours constituted the most delicate test. A further control for this manner of administration might have been carried out, repeating the quantities of 5 grams every six hours on normal individuals. However, where the individual reacts to the first ingestion of 5 grams, it would seem superfluous to repeat this after six hours.

Naturally there is no mathematical proportion between the tolerance to sodium bicarbonate and these small quantities of acetone and oxybutyric acid which were obtained after two or three days of carbohydrate starvation. However, in the spontaneous acidoses of high grade which occur in diabetes, it would appear that, in general, when the quantities of β-oxybutyric acid are high, the body will take up proportionally large amounts of carbonates. The exact relationship of these two factors does not appear to have been studied closely, but apparently there are no exceptions to the general parallelism.

The tolerance tests are certainly not as simple as the determination of acetone for the detection of slight grades of acidosis in well-known conditions, such as starvation. Their advantage would appear to lie in the possibility of their application in some of the clinical conditions in which acidosis is suspected but in which definite evidence is lacking.

An opportunity does not ordinarily present itself for the determination of the order in which the various signs of acidosis appear. A general classification can be made, however, by observing the signs which are found in various stages of acidosis.

Among the earliest signs of starvation are the appearance of acetone and an increase in the acidity of the urine.

This is followed very closely by the appearance of acetoacetic and β-oxybutric acid and, presumably, by the neu-

[6] Sherman and Gettler: J. Biol. Chem., Balt., 1912, XI, 323.

tralization and excretion of the fixed bases and a rise in the tolerance to bases.

The exact position of the ammonia coefficient is a little hard to determine. While its increase may begin rather early, nevertheless, it does not reach a point which is definitely abnormal until the preceding signs are fairly well marked.

The most prominent of the later changes are the diminished alkalinity of the blood as determined by titration, its decreased carbon dioxide content and the development of air hunger.

Pathologic Conditions.—In the selection of pathologic material for study, those conditions were chosen in which an acidosis, due to other than β-oxybutyric acid, may be suspected. Especial attention was given to some of the different types of nephropathies. Diabetic cases of a certain type were also studied. It will be remembered that Naunyn has emphasized the possibility of the occurrence of other acids in addition to β-oxybutyric in diabetes. We have sought for such evidence by applying the tests for tolerance to sodium bicarbonate in suitable cases.

One case representing an obscure toxæmia of pregnancy is also discussed, since it illustrates certain theoretical considerations in connection with acidosis.

Diabetes.—In looking for evidence of acids which do not commonly occur in diabetes, patients were selected in whom the urine did not show acetone and acetoacetic acid. Three were studied who were excreting sugar freely when on a mixed diet and two others who showed an intermittent glycosuria. The general results are shown in Table IV.

TABLE IV.

SHOWING THE BEHAVIOR OF THE EARLIER STAGES OF DIABETES TOWARD SODIUM BICARBONATE.

Case No.	Weight (lbs.).	Sugar excretion on mixed diet (grams per day).	Tolerance to carbohydrate (grams white bread per day).	Acidity in % of N/1 solution.	Ammonia coefficient.	Total acetone (grams per day).	β-oxybutyric acid (grams per day).	White bread in diet (grams per day).	Sugar excretion (grams per day).	Tolerance to sodium bicarbonate.	
										Grams.	Effect on urine.
1	130	35	175	5.3	5.6	0.011	0.014	150	0	40 in 30 hrs.	Alk. 9 hrs.
2	110	(*)	(*)	3.0	2.6	0.023	0.061	170	0	30 in 30 hrs.†	Alk. 12 hrs.
3	140	120	100	3.6	5.8	0.085	0.259	200	26	10 in one injection.	Alk. 9 hrs.
4	145	25	100	6.3	6.4	0.010	0.083	(§)	25	30 in 12 hrs.‡	Faintly ac. 3 hrs.

* Intermittent glycosuria.
† By ingestion 5 grams every 6 hrs.
‡ By ingestion 10 grams every 6 hrs.
§ Mixed diet.

In addition to the cases in Table IV, a fifth patient, showing intermittent glycosuria, was tested at a time when the urine was free from acetone and sugar. The ingestion of 10 grams of sodium bicarbonate in one quantity brought about an alkaline reaction of the urine which persisted for 15 hours.

Of the four cases in the preceding table it is seen that none of them exhibited definite signs of acidosis as tested by the ordinary methods. In regard to the tolerance for sodium bicarbonate the third case showed no definite increase. The conditions under which the second case was tested suggest at least a slight increase above the normal, but this case was complicated by a heart lesion of sufficient extent to contraindicate any intravenous work. The first and fourth cases afford proof of a distinct increase. Subsequent examinations were carried out in order to determine whether the results would be consistent on repetition. The results were as follows:

The second patient after an interval of 18 days was given 5 grams of sodium bicarbonate by mouth every 2 hours. Twenty-five grams were required to bring about an alkaline reaction of the urine.

In the third patient, after an interval of 10 days, the ingestion of 10 grams of sodium bicarbonate in one quantity brought about an alkaline reaction of the urine which persisted for 6 hours. After another interval of 10 days, 5 grams of sodium bicarbonate was given by mouth every three hours. After the administration of 10 grams the urine became faintly alkaline for 3 hours.

The test was not repeated in the fourth patient. In the first patient several repetitions were made by intravenous injections. The results are shown in the following outline.

REPETITIONS OF THE INTRAVENOUS INJECTIONS OF BICARBONATE IN CASE I.

CASE I.

Interval between tests.	Ammonia coefficient	Total acetone (grams per day).	β-oxybutyric acid (grams per day).	Tolerance to sodium bicarbonate.	
				Grams.	Effect on urine.
....	5.6	0.011	0.014	40 in 30 hrs.	Alk. 9 hrs.
8 days	6.0	0.010	0.050	40 in 30 hrs.	Alk. 8 hrs.
5 days	5.7	0.018	0.041	30 in 18 hrs.	Alk. 7 hrs.

These data show that the results in Table IV, as far as they have been tested, were consistent on repetition. The behavior of the first and fourth cases was rather unexpected. These two patients had noticed symptoms over a period of several years; it might be supposed that their abnormal reaction toward sodium bicarbonate had required a relatively long period for its development and that perhaps this condition would return only after a long interval. The preceding outline, however, shows that, at least in the first case, a few days were sufficient to permit its return.

A comparison of these two cases (Nos. 1 and 4) showing an increase in tolerance with the one (No. 3) whose tolerance is normal is somewhat instructive. Here we have three men, in a similar stage of diabetes. None of them represents the adipose type of the disease. All excrete sugar freely but become sugar free when the carbohydrate intake is moderately reduced. No definite signs of acidosis are present, the excretion of acetone being normal, and the ammonia not being significantly increased. Yet, their behavior toward sodium bicarbonate is radically different. The only indication of this difference consists in the subjective symptoms of which these men complained. The two who showed a well-marked in-

crease in tolerance toward bicarbonate had developed symptoms referable to the nervous system. The first one came to the hospital asking for treatment for symptoms of ataxia,[7] and the other for symptoms indicating an early multiple neuritis. The third case showed no signs of any involvement of the nervous system and complained primarily of the usual symptoms referable to starvation and glycosuria, but he also spoke of pains in the legs and muscles.

In the course of a year only two cases of this first type have been observed. It will prove of more interest and importance if this condition is fairly common, rather than if it is an unusual occurrence. In considering its explanation it is important to note that no signs of nephritis were present. Otherwise one might think of the possibility of the retention of bicarbonate on account of defective kidney function. If one assumes that some unknown acid is responsible for this behavior, then it would seem that the disproportion is rather great between the production of ammonia and the behavior toward the bicarbonate.

Certain other considerations arise which are of theoretical interest. The data in Table I indicate that under normal conditions the body contains almost the maximum amount of fixed bases which it is capable of assimilating, *i. e.*, even when small amounts are presented to it by injection, or by way of the alimentary tract fixed bases promptly appear in the urine. One may inquire, therefore, as to the total quantity of the reserve supply of fixed bases which the body possesses and the extent to which this supply may be depleted before symptoms appear. It is certain that well-marked degrees of acidosis frequently develop without the appearance of definite subjective symptoms. Nevertheless, the replacement of these bases is such a simple matter that it would seem to be a desirable step. In the two patients under consideration it would seem that a deficiency of bases existed, in moderate degree, and under conditions in which it would not be detected by the tests on which one ordinarily relies.

Toxæmia of Pregnancy.[8]—The tolerance exhibited by the cases of diabetes is of especial interest when compared with the results obtained in an obscure toxæmia of pregnancy. The essential features were as follows:

In the third month of pregnancy, pernicious vomiting developed. The ammonia coefficient was high, varying usually from 30 to 35 per cent and these values persisted notwithstanding the introduction of glucose by rectum. A hysterotomy was performed promptly, but without any permanent improvement in the general condition of the patient. On the day following the operation the ammonia coefficient fell from 34.5 per cent to 22.1 per cent, but rose rapidly, eventually reaching 40 per cent. Little food was retained by mouth, but quantities of 75 to 100 grams of glucose per day were given by rectum and the absorption was apparently good. Qualitative tests showed the presence of acetone in the urine. The tolerance to sodium bicarbonate was tested and quantitative estimations were made of the total acetone and β-oxybutyric acid, in order to obtain evidence of the extent of any starvation acidosis which might be present. These tests were made one week after operation. The results were as follows:

Intravenous Injection of 6 Grams of Sodium Bicarbonate.

Interval between tests.	Acidity of urine.*	Ammonia coefficient	Total acetone (grams per liter).†	β-oxybutyric acid (grams per liter).†	Effect on reaction of urine.
....	2.5	32.2	0.248	0.021	Alk. or neut. 42 hrs.
2 weeks	2.0	30.0	.....	.....	Alk. 6 hrs.
1 day	1.5	31.9	0.095	0.162	Alk. or neut. 42 hrs.

* Per cent of normal solution.
† The absolute values are not available on account of some incontinence. There was a free excretion of urine however; the daily quantities averaged about 1½ to 2 liters. The absolute quantities of ammonia were not greatly increased, the values varying from 0.6 to 1.4 grams per liter.

The values for β-oxybutyric acid fall within the normal limits of Shaffer's method. The increase in the ammonia coefficient is many times greater than could be accounted for by the slight increase in acetone. The tolerance to sodium bicarbonate is normal. This is in marked contrast to the diabetic patients who showed a normal amount of acetone and no significant increase in ammonia, but a high tolerance to sodium bicarbonate.

There are two factors which might have a bearing on this seeming paradox. In the diabetic cases one must consider the possibility of the occurrence of an unknown acid which had withdrawn fixed bases from the body.

The most plausible explanation of the data obtained in the toxæmic case is that the condition was not a starvation acidosis, but was essentially a primary disturbance of protein metabolism. Theoretically, therefore, the tolerance to sodium bicarbonate in this case would not be increased even though acetone, acetoacetate and β-oxybutyrate were being excreted freely, since the increase in ammonia production was proportionally much greater than the quantities of acid which were produced. The essential feature which this case illustrates is that an increase in the excretion of ammonia and of acetone and its related bodies does not necessarily indicate a disturbance in the equilibrium between acids and bases and it is not always accompanied by a rise in tolerance to sodium bicarbonate.

Nephropathies.—The study of renal diseases in connection with acidosis is of interest from two standpoints. In the first place one must consider whether any of the various nephropathies may interfere with the excretion of substances by which acidosis is ordinarily recognized, and whether in the use of sodium bicarbonate one might find retention of this salt on account of disturbance of the kidney function. On the other hand, the conception has frequently been advanced that nephritis and especially uræmia may be essentially an acidosis. Various findings have been noted which lend more

[7] A definite Romberg sign was not present and the Wassermann and luetin reactions were negative.

[8] I take pleasure in acknowledging the kindness of Dr. J. W. Williams for the privilege of following this case which occurred in the obstetrical service of this hospital. I am also indebted to his staff for many favors and especially for the data on the ammonia metabolism.

or less support to this view. Many observers report a reduction in the alkalinity of the blood. β-oxybutric and other organic acids have been found in the urine. Recently Straub and Schlayer[9] have reported a diminution in the carbon dioxide content of the alveolar air. Senator has been especially prominent among those who have laid emphasis on the possible relation between acidosis and uræmia. von Noorden, however, considers that, although a slight grade of acidosis may be present in uræmia, it represents merely an effect and not the underlying cause of the condition. The consensus of opinion is in agreement with this latter view.

In the application of the sodium bicarbonate tests, in the presence of kidney lesions, the first step evidently consisted in the determination of whether any of the various nephropathies behaved in an abnormal manner toward the introduction of sodium bicarbonate into the body.

In the adoption of a routine for the examination of kidney cases it seemed especially important to carry out the ordinary tests for the detection of acidosis. For this purpose I have depended principally upon the ammonia coefficient and the determination of acetone and oxybutric acid. These two latter examinations seemed necessary in order to control the possibility of a starvation acidosis and also on account of the occasional occurrence of these substances in uræmia.

In addition the test of renal function by phenolsulphonephthalein is also recorded.[10]

No patients were chosen in whom cardio-renal conditions existed, except those in which the cardiac lesion was well compensated and the question of a stasis kidney could be eliminated. For the most part fairly simple cases were selected which corresponded more or less definitely to certain general types of renal lesions. In view of the confusion which exists in the transition from the older ideas to the newer views regarding renal disease it has been difficult to adopt a satisfactory terminology. For example, there is considerable uncertainty as to whether chronic interstitial nephritis is really an inflammatory process and for this reason the more general term "nephropathy" has been used in this paper. In many of the cases which were studied there was evidence of a diffuse involvement of the kidney. Those in which the signs of glomerular lesions predominated are classified in the parenchymatous group while the arteriosclerotic and primarily contracted kidneys are included under the designation of chronic interstitial disease.

The results are given in Table V.

Some supplementary data are necessary concerning the more important cases in the preceding table.

Case No. 1. Ten days before this injection this patient received two injections of 10 grams each of sodium bicarbonate in 2 per cent solution with an interval of 8 hours between the injections. The urine remained acid. This result would have been conclusive of an increase in tolerance

[9] München med. Wochen., 1912, lix, 569.

[10] The writer is indebted to Dr. Rowntree and Dr. Fitz of this university for their kindness in supplying these data from their studies in renal function.

TABLE V.

EFFECT OF SODIUM BICARBONATE ON THE REACTION OF THE URINE IN VARIOUS NEPHROPATHIES.

Case No.	Weight (lbs.).	Type of nephropathy.	Ammonia coefficient (per cent).	Total acetone (grams per day).	β-oxybutyric acid (grams per day).	Administration of sodium bicarbonate.	Reaction of urine to litmus.	Phenolsulphonephthalein output. First hour.	Phenolsulphonephthalein output. Second hour.
						Intravenous injection.			
1	175	Chr. interstitial..	3.6	0.016	0.026	16 gms. in 8 hrs.	Ac.....	24 %	(1)
2	135	Chr. diffuse.....	(2)	20. 07	2 0.093	40 gms. in 24 hrs.	Ac.[3].....	2 %	5 %
3	170	Acute nephritis with uræma.	2.0	0.026	0.010	130 gms. in 66 hrs.	Ac.....	(4)	
4	155	Acute exacerbations of chr. parenchymatous.	2.4	0.012	0.076	10 gms. in one injection.	Alk. 24 hrs..	15 %	45 %
5	140	Chr. parenchymatous.	6.4	0.020	0.056	10 gms. in one injection.	Alk. 18 hrs..	5 %	10 %
6	180	Chr. diffuse nephritis with uræmia.	4.4	0.023	0.052	60 gms. in 24 hrs.	Ac.....	Trace.	Trace
7	155	(5)	2.4	0.021	0.022	20 gms. in 20 hrs.	1 alk. specimen.	....	
						Ingestion tests.			
8	130	Chr. diffuse.....	...	0.015	0.055	6 10 gms. in 6 hrs.	Alk. 4 hrs...	7 30 %	
9	190	Chr. diffuse.....	11.2	0.054	0.045	8 30 gms. in 15 hrs.	Ac.....	....	(9)
10	145	Chr. diffuse.....	1.7	0.013	0.030	8 30 gms. in 15 hrs.	Ac.....	....	(10)
11	125	Chr. nephritis with diabetes.	6.4	0.006	0.030	8 30 gms. in 15 hrs.	Ac.....	17 %	27 %
12	100	Chr. diffuse.....	(2)	.....	.....	6 40 gms. in 42 hrs.	Alk. 3 hrs...	Trace.	10 %
13	165	Chr. parenchymatous.	...	.....	.....	5 gms.....	Alk. 6 hrs...	47 %	79 %
14	145	Chr. parenchymatous.	...	.....	.....	6 10 gms.....	Alk. 6 hrs...	23 %	45 %

[1] A total of 60 per cent in 3 hrs.
[2] Ammoniacal fermentation in lower urinary tract.
[3] After heating.
[4] A total of 10 per cent in 4 hrs.
[5] Albuminuria in acute rheumatic fever.
[6] 5 grams every 6 hours.
[7] By intravenous injection.
[8] 5 grams every 3 hrs.
[9] A total of 30 per cent in 3 hrs.
[10] A total of 30 per cent in 2 hrs.

except for the existence of a slight acetonuria arising from a very restricted milk diet. The urine on the day preceding the injection did not give the qualitative tests for acetone. On the day of the injection the sodium nitroprussid color reaction was suggestive, but the ferric chloride test for acetoacetic acid was negative. Carbohydrates were supplied freely during the interval between the first and second injections. The sodium bicarbonate was used in 2 per cent solution, 500 cc.[11] being introduced at one time. The blood pressure in this patient was high, averaging about 180 mm. of mercury. This quantity of fluid, however, could be introduced, not only without raising the pressure, but it was usually accompanied by a fall of about 30 mm. developing within a few hours and lasting 12 to 18 hours.

Case No. 2. In this patient there was a long standing infection of the lower urinary tract, resulting in ammoniacal fermentation of the urine. In order to determine whether any carbonates were being excreted, samples of urine were concentrated in an evaporating dish over the free flame. When no fixed base was present, the ammonia was soon driven off and the acid reaction of the urine returned. In the same manner, when normal urine is made alkaline with dilute ammonia, the excess of ammonia is driven off on boiling and apparently the ammoniacal salts, formed from the neutrali-

[11] Except in the second injection of the test which is recorded in Table V.

zation of the acid phosphates, are decomposed with loss of ammonia, since the urine becomes not neutral, but acid in reaction. When much fixed base is present, the vapors do not become ammonia free on boiling, on account of the decomposition of urea; however, this does not give rise to any confusion.

These tests were also confirmed by drying and heating litmus paper in the usual manner for distinguishing between ammonia and the fixed bases.

This patient received quantities of 10 grams at each injection in 2 per cent solution. The first injection was followed by a chill with slight rise in temperature accompanied by subjective discomfort. These reactions increased in severity with each injection, and accordingly the bicarbonate was discontinued before any had been excreted in the urine.

Case No. 3. Other important factors in addition to the uræmia were present in this case. The nephritis developed as the result of infarctions from a subacute infective endocarditis. The observations were carried out during a practically afebrile period.[12] This would not be sufficient to exclude a febrile acidosis, inasmuch as this short period had been preceded by a febrile course lasting several weeks. However, if a febrile acidosis did exist, it was of such a type that it could not be detected by the ordinary tests, such as an increase in the ammonia coefficient or the excretion of acetone. A positive Wassermann reaction was obtained, but this was the only evidence of syphilis.

This patient had been under observation in the ward for one week. At the time of the first injection the symptoms of uræmia were fairly definite. None of the usual signs of acidosis were present. There was a gradually increasing dyspnœa. The respirations were moderately deep and free; the rate varied from 28 to 36 per minute. The mucous membranes were bright in color, although the hæmoglobin and the red blood count were low. On one occasion the patient called repeatedly for "air," and when questioned he said that he had no pain, but could not get his breath. There were no physical signs in the lungs at this time to account for this symptom.

Twenty grams of sodium bicarbonate in 2½ per cent solution were given at the first injection. Three injections were made in the next 32 hours. Quantities of 20 and 30 grams were introduced at one time, increasing the concentration to 4 and then to 5 per cent. The respiratory rate fell to 18 and even as low as 14 per minute. At times there was definite Cheyne-Stokes' respiration. Muscular twitchings of the face and the upper extremities also developed. These were not extensive, involving only one or two movements at a time. They persisted intermittently until death, but intervals of several hours frequently occurred in which no twitchings appeared. A localized œdema developed in the left hand. The veins at the elbow on this side had been used repeatedly for injections and withdrawal of blood specimens, but there were no evidences of thrombosis. In the next 24 hours the œdema diminished markedly.

A specimen of blood serum taken after the fourth injection of bicarbonate did not show any increase in the alkalinity as measured by titration with N/10 acid against dimethyl-amido-azobenzene. An additional injection of 30 grams was given. The injections were then discontinued, inasmuch as the dyspnœa did not return and there was no indication that an alkaline urine could be obtained or that a polyuria could be produced. A distinct oliguria persisted, though anuria did not develop. Death occurred 32 hours later.

The autopsy[13] showed extensive infarction of the kidneys accompanied by an acute diffuse nephritis. Microscopically the involvement of the glomeruli was very general. The interstitial tissue was nowhere increased, but accumulations of mononuclear cells were scattered throughout the renal tissue in greater abundance than normal. The blood vessels were everywhere congested.

Case No. 6. This patient was a chronic nephritic in uræmia. Œdema was well marked, especially over the lower extremities. A satisfactory response was not obtained to any therapeutic measures. Sixty grams of sodium bicarbonate in 24 hours, divided into three injections of 20 grams each, failed to change the reaction of the urine. Titrations made before and after the injections of bicarbonate showed no diminution in the degree of acidity. The œdema was not influenced. Fair quantities of urine were passed until the time of death, which occurred 24 hours after the last injection.

At autopsy the kidneys were found to be slightly enlarged. A chronic diffuse nephritis was present. Microscopical examination showed a uniform increase in fibrous tissue. The glomeruli were large; the uriniferous tubules were atrophic in places while in other areas they were dilated and lined by a low epithelium. The blood vessels showed a slight amount of thickening.

Case No. 7. This case showed a marked grade of albuminuria, accompanying acute rheumatic fever, the urine containing 1 per cent of albumin on the day of injection. No casts were present. This patient was introduced into this series on account of the indefinite significance of albuminuria in nephritis. The tolerance to bicarbonate was definitely increased, but this might be interpreted as evidence of a slight acidosis in rheumatic fever.

Case No. 8. This case was a cardio-renal patient. The test recorded in the table was made at the first appearance of symptoms of uræmia and showed that there was no increase in tolerance to bicarbonate. The nitrogen and water output remained good, but death occurred two weeks later, the symptoms of uræmia persisting.

The autopsy showed a chronic and subacute diffuse nephritis. Microscopically the cortex of the kidney was markedly scarred. The glomeruli were prominent; many of them were converted into hyaline masses while others were larger than normal and very cellular. The tubules were lined by a low cubical epithelium which was coarsely vacuolated and in some places it was granular. The interstitial tissue was increased in patches and in such areas

[12] Blood cultures made by Dr. Major showed that the *Streptococcus viridans* was present in considerable numbers during this period.

[13] The notes upon the autopsy findings in these three cases were furnished very kindly by Dr. Winternitz.

the tubules and glomeruli showed retrogressive changes. The fibrous tissue increase was characterized further by an infiltration of mononuclear cells. The blood vessels showed thickening of their walls in the region of the fibrosed areas but otherwise they were not markedly involved.

Case No. 9. This is the only instance in which a high ammonia coefficient was obtained. A subsequent test five weeks later gave an ammonia coefficient of 9.5 per cent. This is of comparatively little interest, however, since this case was complicated with hepatic cirrhosis.

Case No. 11. This result can hardly be interpreted on account of the coexistence of diabetes and nephritis; the patient at the time of this test was sugar free. The result is perhaps of some negative value to show that the tolerance in this instance was not normal.

The case also serves to illustrate a situation which may arise in the handling of diabetic patients. Thus Naunyn has emphasized that the same sclerosis of the blood vessels which gives rise to changes in the pancreas may also involve the kidney and affect the renal function. In this manner the occurrence of diabetes and nephritis in the same individual gives rise to two conditions either of which may increase the tolerance to bases. In diabetic coma it is assumed that the administration of carbonates should be continued until they appear in the urine. However, the same rule is not yet established for the nephropathies. Consequently in an uncomplicated case of diabetic coma the explanation of the persistence of an acid reaction of the urine after the introduction of carbonates may be essentially different from a similar case in which renal lesions are present.

The intravenous injection of bicarbonates in many of the preceding cases was not well borne. Reactions frequently appeared which were similar to those known as "salt fever," following the intravenous injection of physiological salt solution. These reactions were especially pronounced in the two cases of chronic parenchymatous nephritis. The stimulating effect of sodium bicarbonate[14] was observed in some instances. The reactions were severe enough to contraindicate the intravenous injection of bicarbonate except in selected cases. On account of these reactions and in the absence of the explanation of this increase in tolerance, it seemed sufficient to establish whether the tolerance was normal or distinctly increased without attempting to determine the maximum limits of this increase. The two patients (Nos. 3 and 6) who received the largest quantities developed no reaction and experienced no discomfort, except for some stimulating effect seen in the second case (No. 6). Also no disturbances were observed in the ingestion tests following the quantities of bicarbonate which were used.

One feature which seems remarkable is that such large quantities of salt could be introduced in advanced cases of nephritis without any definite influence on the œdema. Though many of the observations in œdema have been made with sodium chloride yet since the effect of the salt is supposedly due to salt action *per se* and not to any specific properties of the ions themselves, the sodium bicarbonate should be only moderately less effective than the sodium chloride.

The one feature which is most prominent in Table V is that a distinct difference exists in the excretion of the carbonates in various types of nephropathy.

In the four cases of the chronic parenchymatous type sodium bicarbonate is readily excreted. This agrees with von Noorden's statement that carbonates are readily excreted in nephritis. Furthermore, the cases which behave in this manner do not support Fischer's[15] views regarding acidosis in nephritis. Indeed the data from the control cases would enable one to exclude acidosis rigidly in these four cases of chronic parenchymatous nephritis except for the theoretical possibility that even in acidosis the parenchymatous nephritic kidney would permit the excretion of bicarbonates under conditions in which, with a normal kidney, the bicarbonates would be retained by the tissues.[16]

In some of the cases, however, there was a noteworthy increase in the amount of bicarbonate which could be administered without affecting the reaction of the urine. There is but one case (No. 6) in which we have a pure nephritis which is free from infections or other complicating factors, and in which we have clear proof of a well-marked increase in tolerance, as tested by intravenous injections. Nevertheless the general behavior of the cases indicates that there are several diverse conditions among the nephropathies in which an increased tolerance may be expected. In addition to the diffuse nephritides, an impression was gained that the arteriosclerotic changes in the kidney were especially likely to give rise to an increase in tolerance. Prominent among the conditions which give a high tolerance are the acute nephritides with typical uræmia. The results of the tolerance tests in the uræmia appearing in Asiatic cholera show a very definite increase. In the present series, the uræmia developing in the course of an infective endocarditis (Case No. 3) would indicate that these results are not specific for Asiatic cholera, but that they occur in other infections. Similarly, the behavior of the case of uræmia which was free from infection (Case No. 6) would likewise indicate that such results were not specific for bacterial infections, but that they occur in other toxæmias.

In the group of nephropathies which show an increase in tolerance to bases the possibility of an acidosis cannot, as yet, be excluded. At present we have gone no further than to attempt to establish the existence of this condition and have not

[14] Dawson: J. Exper. M., N. Y., 1905, VII. 1.

[15] Fischer, Martin H.: Nephritis. 1912. John Wiley & Sons. New York.

[16] Another suggestion may be offered in support of Fischer's hypothesis. The term acidosis, in its accepted sense, has come to mean a more or less general depletion in the available supply of bases in the body. However, it is conceivable that a condition of a very different nature might be brought about by a localized accumulation of free acid in the kidney, for example, resulting in lesions due to the direct action of the acid on the protoplasm of the cells. The plausibility of such an occurrence might be argued from the supposed susceptibility of the kidney to acids and from its functional activity in the excretion of acids in order to spare the other tissues of the body.

yet investigated its explanation. It does not necessarily follow that the injected bicarbonate is retained in the system. With the impairment of kidney function the body may have other means of disposing of an excess of bases; for example, by excretion into the intestine. But if we assume that a considerable portion of the injection is at least temporarily retained, then two possibilities suggest themselves with especial prominence: (1) Acidosis with neutralization of the injected bicarbonate, and (2) retention of the bicarbonate without neutralization. The one factor which speaks most strongly against acidosis is the absence of other signs, such as a high ammonia coefficient. This objection would have still more weight if the excretion of ammonium salts in nephritis were thoroughly understood. Likewise, the subjective disturbances and the febrile reactions which frequently occurred after the injection of bicarbonate may be interpreted as evidence against the idea of an acidosis.

On the other hand, the idea of retention is not altogether simple. It is well known that the diseased kidney retains a variety of substances such as dyes and sugars and certain salts. The mechanism which is involved would appear to be comparatively simple where the substances in question do not react chemically with any constituents of the urine. In the case of bicarbonates which would combine with the acid salts of the urine the problem is more complicated.

Furthermore, inasmuch as one of the normal functions of the kidney consists in the production of acid salts, then on the theory of retention one would be obliged to assume that a lesion of the kidney had brought about an abnormal functional activity as regards the excretion of acids, since the acid salts persist under conditions in which normally a liberal excretion of hydroxyl ions should occur. Indeed if quantities of as much as 50 grams of sodium bicarbonate may be injected into the body and retained without neutralization, then the source of these acid salts in the urine is not readily explained. Furthermore, in one of the cases (No. 8), the kidneys showed extensive diffuse lesions but were able to excrete carbonates readily. However, we are not yet in possession of proof that the kidney in these conditions has become impervious to bases or that it has reached a state comparable to certain cells of the gastric mucosa, for instance, in which only an acid secretion can be produced

Lastly, it should be emphasized that perhaps many factors may be involved in the explanation of a given case and the explanation of different cases may vary widely. Certainly, in many instances, important extra-renal factors may come into consideration. Thus, the nephritis of Asiatic cholera, where the output of ammonia is often very high, may constitute an essentially different condition from the cases reported in the present paper.

Functional Diagnosis and Therapy.—An examination of the data in Table V shows that in all cases in which the tolerance to bicarbonate is markedly increased, the phenolsulphonephthalein output is very low. On the other hand, the excretion of the bicarbonate is practically normal in some of these cases in which the phenolsulphonephthalein test shows a functional insufficiency. It is obvious that there would be many objections to the use of bicarbonate in functional diagnosis. Such a procedure would evidently be less delicate than the phthalein test and it would be complicated by important extra-renal factors.

The study of the majority of substances which are retained by the kidney are of interest from the standpoint of functional diagnosis rather than of therapy. In the case of the bicarbonates, however, the explanation of their behavior might have some bearing on therapy in case it should be shown that they fail to appear in the urine on account of the existence of an acidosis.

The use of the carbonates in the treatment of nephritis has assumed some prominence of late. v. Hösslin [17] reports a reduction in albuminuria following a reduction of the acidity of the urine by the use of sodium bicarbonate. He also noted a marked variation in nephritics in the amount of bicarbonate required to effect a reduction in the acidity of the urine. He administered sodium bicarbonate by mouth in quantities varying from 2 to 15 grams and in one case 24 grams per day. Its use was continued over periods varying from two to four weeks. The acidity of the urine was titrated according to Moritz's method, and from the figures which are given it would appear that, in many instances, the reaction probably became alkaline to litmus. v. Hösslin found many instances in which the albuminuria was not influenced, but recommends that bicarbonate in increasing doses should be tried in all cases of nephritis.

Fischer [18] has recommended the normal carbonate and the results reported indicate a rapid diminution in the albuminuria, a pronounced diuretic action, and a striking improvement in the general condition of the patient.

Perhaps the most hopeful conditions for treatment are those infections in which an acute nephritis may be anticipated and measures may be instituted before its actual development occurs. However, it is certainly desirable to approach the question from something more than an empirical basis.

I am inclined to think that one of the most important factors to determine is whether changes do occur in the kidney which render it incapable of excreting anything but an acid urine even after the introduction of an excess of bicarbonate into the body.

Summary.

The tolerance of the body toward fixed bases has been studied by determining the amount of sodium bicarbonate which must be introduced into the body in order to render the urine alkaline. The following results have been obtained:

In normal individuals the ingestion of five grams of sodium bicarbonate is ordinarily sufficient to bring about the excretion of fixed bases in the urine, its reaction becoming alkaline, though in exceptional cases, this quantity of bicarbonate is insufficient, 10 grams being necessary.

[17] Deutsches Arch. f. klin. Med., Leip., 1912, CV, 147.

[18] Fischer: Loc. cit.

The tolerance to sodium bicarbonate was tested in acidoses produced artificially, in five cases of diabetes, in an obscure toxæmia, accompanied by an increased excretion of ammonia, and in a group of thirteen nephropathies.

A slight grade of acidosis, resulting from a carbohydrate free diet for a period of two to three days produced a small but definite rise in the tolerance to bicarbonate. A similar result was obtained in two cases by the ingestion of small quantities of a mineral acid.

In the five patients with diabetes who were tested, the ordinary signs of acidosis were absent. In three of these patients the tolerance was normal; in two, however, it was definitely increased, the urine remaining acid after the administration of 30 grams of sodium bicarbonate.

In the toxæmic case in which the ammonia excretion was increased there appeared to be a primary disturbance of protein metabolism rather than an acidosis, with a secondary increase in ammonia. The tolerance in this case was normal.

In the study of 13 patients representing several types of nephropathies it was found that four comforming to the general type of a parenchymatous nephritis excreted carbonates, readily behaving in this respect like normal individuals. Consequently the tests on this group do not afford evidence of an acidosis, at least not in the generally accepted sense of the term.

One patient with chronic diffuse nephritis also showed a normal tolerance but none of the remaining patients behaved in a normal manner. Two patients continued to excrete an acid urine after the intravenous injection of sodium bicarbonate in quantities of 60 and 130 grams respectively.

Discussion.

The determination of the tolerance of the body to sodium bicarbonate appears to afford a basis for the development of a method of general application for the detection of acidosis. As far as the clinical interpretation is concerned, it would seem that essentially the same result is obtained by either the intravenous injection or by the ingestion of bicarbonate. Evidence was obtained which indicates that the tissues of the body possess the property of taking up sodium bicarbonate very readily even in the early stages of an acidosis. This may be interpreted as indicating that a slight increase in the acid metabolism is compensated for, in part, by the fixed bases of the body and not wholly by an increase in the excretion of ammonia and of acids.

The interpretation of the ammonia metabolism and the study of the tolerance to sodium bicarbonate are affected in a very different manner by certain conditions which may complicate the detection of an acidosis. Thus an increase in the excretion of ammonia may occur not only in an acidosis but also as the result of a primary disturbance of protein metabolism. In the case of renal lesions, however, the data which are available in the literature indicate that there is no retention of ammonia, and accordingly a nephritis would not interfere with the study of the ammonia excretion. On the other hand, the test for the tolerance to sodium bicarbonate is readily applicable in the presence of disturbances of protein metabolism but the effect of kidney lesions is very obscure. From the limited number of cases reported in this paper it would seem that the one group of nephropathies which do not interfere by reason of the retention of carbonates are those cases which conform to the general type of chronic parenchymatous nephritis. The nephropathies in which the tolerance is increased would interfere with the test if this tolerance is due to retention of bicarbonate on account of the renal lesions.

In the attempt to obtain some evidence concerning the equilibrium between acid and base in the body, many methods have been suggested for the determination of the alkalinity of the blood. However, it would seem that, during pathologic processes when the body is becoming impoverished in certain constitutents, the composition of the blood may be maintained in a relatively normal condition at the expense of the other tissues. For example, when a diminution occurs in the content of the body in carbohydrates or in water, the blood is supplied from the other tissues until their supply is seriously depleted. It seems not unlikely that the same considerations apply in the case of the fixed bases. Consequently, the determination of the tolerance to bicarbonates may afford some information concerning any deficiency which may exist in the content of the tissues in fixed bases; such evidence would be of a very different nature from that obtained by the determination of the reaction of the blood.

In conclusion, I wish to express my appreciation to Prof. L. F. Barker for assistance and for an interest in this work which has been very valuable.

EMBRYONIC BANDS AND MEMBRANES ABOUT THE CÆCUM.

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Some four years ago, under the name of membranous pericolitis, Jackson called attention to what he believed was a distinct form of pericolitis, a definite pathological and clinical entity. This condition is characterized, according to Jackson, by the formation of an entirely new layer of vascularized peritoneum, which is found usually on the ascending colon, often extending up to the hepatic flexure and over on to the transverse colon. In a second report, the original account of the condition has been amplified by the description of an autopsy specimen by Hall, from whose notes the following points are excerpted:

Running from a point near the hepatic flexure to a point three inches above the caput cæci and extending from the parietal peritoneum to the lateral and ventral aspects of the colon, is a thin

vascular veil with long, straight, parallel, unbranching vessels. The appendix is not implicated in any way. With the blood-vessels are long shining bands of connective tissue which gradually broaden and spread out in slight fan-shaped attachments on the anterior and inner surfaces of the colon. The latter is freely movable beneath this membrane. On section, there is no evidence of inflammation, but one finds numerous endothelial lined spaces which suggest a chronic lymph stasis.

While we owe to Jackson the recognition of the possible pathological significance of these membranes, as well as their first accurate description, they have undoubtedly been seen by other observers previous to his report. To Virchow, Hofmeister ascribes the first description, while it is certain that Binnie and Lane had also observed similar structures prior to Jackson's paper.

Since that time cases of so-called membranous pericolitis have been reported by Hofmeister, Connell, Crossen, Pilcher and Gerster, as well as an additional series by Jackson.

The symptoms with which these patients, reported in the literature, suffer may, in general, be classified with those that are already familiar to us in certain types of chronic appendicitis. Pain is ordinarily the thing which makes them seek medical advice. It varies in intensity from feelings of discomfort to a more or less continuous pain on the right side, usually most marked in the right lower quadrant. It is liable to exacerbations and not infrequently accompanied by colic. Tenderness is usually greatest over the cæcum, although palpation may elicit more or less definite response over the entire right side of the abdomen. The patients are usually constipated, especially in advanced cases, although Gerster's series contains several with diarrhœa. The stools may contain mucus, and not infrequently there are gastric symptoms in a sense of fullness after meals with eructations similar to those in appendiceal dyspepsia. Some of the cases have been in undoubted abdominal neurasthenics.

Etiology.

Concerning the etiological factors involved in the formation of these veils, there have been numerous speculations on the part of those who have reported cases. Jackson, to whom we owe our recent interest in them as possible pathological entities, does not venture to ascribe a cause to their formation.

Lane, in discussing the fixation of the cæcum, describes acquired lateral adhesions passing in from the abdominal wall to the cæcum, ascending colon and, in some instances, the proximal portion of the appendix. He states that "The portion of the cæcum above the brim of the pelvis, together with the ascending colon, is retained in a position of abnormal fixity to the posterior wall of the abdomen. This is affected by the development of adhesions between the outer aspect of the large bowel and the peritoneum covering the abdominal wall in its vicinity. In advanced cases, these adhesions are supplemented by a mesentery in which vessels of some size are contained. As a rule these adhesions merely fix the bowel, but occasionally they constrict its lumen very materially in one or more situations and render it liable to become obstructed. Not only do these adhesions anchor this part of the large bowel, but they also bind down to the iliac fossa a portion of the appendix." It is quite certain from this description that the acquired adhesions and mesentery of Lane are identical with the veil described by Jackson.

Binnie considers the membrane to be due to a primary colitis, and that the appendix, if involved, is secondary. Hertzler views them as inflammatory in origin and secondary to affections of the appendix or gall-bladder. These views coincide with those of Hofmeister, who, likewise, looks upon them as structures arising from inflammation in adjacent organs, such as the duodenum, biliary passages, appendix or gall-bladder. Connell, on the other hand, does not regard them as inflammatory in origin, but due to ptosis of the cæcum.

According to Charles Mayo the veils result from "a late rotation of the bowel and descent of the cæcum from its hepatic position after the formation of the parietal portion of the peritoneum in the infant. The cæcum burrows its way into position, as it were, through the peritoneum."

In a recent communication Pilcher expresses himself as follows: "As to the etiology of these films and bands, that view which considers them to be the result of long continued or oft repeated mild infections of the peritoneal coverings of the cæcum and appendix transmitted through the intestinal wall seems to me most probable," while Gerster, the latest contributor on the subject, expresses the view that, "The peritoneum reacts to the infectious processes ordinarily associated with chronic colitis, by the formation of characteristic vascularized transparent membranes (pseudoperitoneum), which take their origin along the external aspects of the cæcum, ascending colon and hepatic flexure."

An analysis of the views expressed by the various contributors to this subject is interesting, for, while there is no question that they are discussing the same structures, yet there is a wide divergence in their opinions as to both the origin and nature of the membranes. Suggestions varying from folds of peritoneum caused by the cæcum burrowing behind the parietal peritoneum in a delayed descent (Mayo), and acquired adhesions to prevent the ptosis of the cæcum (Lane), to various inflammatory or infectious etiological factors (Pilcher, Hofmeister, Binnie, Gerster), have been given as the essential basis of their formation. As it is important for us to know both the origin and the pathological significance of these veils, we have accordingly made it a routine to study carefully the cæcum and ascending colon, with this object in view, whenever we have had access to the right half of the abdomen.

During the past two years I have met with some 29 instances where pericolic membranes of one form or another were found at operation. A detailed account of the histories and findings in these cases would make this paper too voluminous, so simply a summary of the results obtained by a study of these patients will be presented. The pericolic membranes vary widely in their position and distribution, but in almost every instance their physical characteristics are the

same. These fine, filmy structures were well described by Jackson in his first and second papers and to his description of their gross appearance there is little to be added.

So far as their general characteristics are concerned, they are fine, delicate membranes extending over the surface of the first part of the large intestine, which is freely movable under them. They give, as Hall has aptly pointed out, the impression as though the colon were placed in a thin diaphanous bag slightly too small for it. The cobweb veil is very thin and is covered by glistening peritoneum and contains numerous characteristic parallel blood-vessels, which run for a considerable distance without anastomosing. They originate from the vessels of the parietal peritoneum and usually run downwards and forwards to terminate by communicating with the vessels in the muscular coat of the intestine. The attachments of the membranes to both the parietal peritoneum and the intestine are extremely loose and elastic. Here and there, there are firmer strands of connective tissue and the veil terminates usually by spreading out in fan-shaped processes or extensions as it insensibly loses itself in the peritoneal surface of the intestine. The membranes are paper thin and only now and then do they show any deposits of fat. The impression given by them is quite different from that ordinarily conveyed by pathological adhesions. They are neither as opaque nor as avascular as adhesions, and they have, in general, a more or less regular distribution. They are, moreover, much thinner than the parietal peritoneum, as is easily seen when traction is made upon them, for the parietal peritoneum that is pulled out at the points of attachment has the thicker, more opaque appearance that is always seen in hernial sacs.

The histological studies of Hall on this structure, while confined to a single specimen, are accurate and his conclusions that the membranes are not inflammatory seem quite justified.

So far as their distribution is concerned, we have found from our series of cases that they may roughly be divided into three groups. The commonest group is that where the veil extends from the parietal peritoneum along the lateral margin of the colon, particularly near the hepatic flexure, over onto the lateral and ventral aspects of the colon and cæcum. Often the caput of the cæcum is free, but they may extend downwards not only to the caput, but even cover the proximal portion, and sometimes the entire appendix as well.

Another type occurs lower down and extends from relatively the same part of the parietal peritoneum over onto the head of the cæcum and usually covers the proximal half and more rarely the entire appendix. Veils of this description do not, as a rule, extend high up on the ascending colon.

The third type of veil, which is relatively rare, extends from the ventral aspect of the colon and passes over and is continuous with or apparently adherent to the omentum. In some cases, it may extend from the parietal peritoneum on the lateral wall of the abdomen over the ascending colon and then become continuous with the omentum, often holding the ascending and the first part of the transverse colon side by side with a sharp angulation at the hepatic flexure if the latter happens to be long and looped.

Between these three main types of veil there may be intermediate stages or combinations of two types. In fact, each case differs somewhat from the next, but in any considerable number of instances, they will fall more or less naturally into these three groups.

Before we take up the consideration of the nature of these membranes it may be well to consider for a moment the usual peritoneal attachments of the colon and cæcum. In a large percentage of cases, these veil-like structures will be observed about the hepatic flexure, frequently shading off into the omentum, or else making up the supporting reflexion of the peritoneum which extends from the hepatic flexure and over onto the kidney. Likewise, along the lateral and posterior aspect of the ascending colon, tissue, similar in structure to the membranes, will be found holding it (the ascending colon) in place.

Turning, for a moment, to the embryology of this portion of the alimentary tract, the following brief account of the development of the topography and attachments of the first portion of the large intestine, affords the only means by which the origin of these membranes can be explained.

After the reversal or rotation of the gut, the cæcum comes to occupy a position just under the liver about the final site of the hepatic flexure. When the rotation is complete, the mesogastrium balloons forward and the formation of the great omentum begins. This fuses later with the transverse colon and the gastro-colic omentum thus comes into existence. Usually this fusion takes place only along the transverse colon, establishing the usual relationships. Not infrequently, the omental attachments extend further to the right, even to the abdominal parietes. After the cæcum takes up its subhepatic position, there is a fusion between the peritoneal surfaces of the cæcum and the posterior abdominal wall, attaching the large intestine in its new position. As the cæcum descends with the subsequent formation of the ascending colon, the posterior surface of its mesocolon also becomes adherent, thus obliterating the free mesentery of this part of the large intestine. This brief description of the development of the attachments and position of the first segment of the large bowel is of the more frequent types, but here, as elsewhere in the body, we have frequent variations in form, connections, and relationships, as can be seen by studying any large series of cases. Variations in the positions, attachments, time of rotation, and descent are particularly common in this region, as is shown by Smith's study of the relationship of the large bowel in one thousand infants. Now, concerning the nature and position of attachments of the colon to the abdominal wall, we have no careful anatomical studies. Furthermore, embryologists do not possess much detailed information concerning the exact nature of the secondary fusion that takes place between the various layers of the peritoneum, such as the obliteration of the mesentery of the ascending colon and the formation of the attachments of the first part of the large intestine in its final position.

With the usual topography and peritoneal reflections of this part of the large intestine, we are all familiar, as this is what we are accustomed to call the norm. In reality, however,

this is only the predominating type and there are series of less frequent forms which, however, should not be looked upon as pathological, but rather as variations common enough to classify as normal. A study of these less common types, particularly during the stage of their formation and with particular reference to the attachments of the cæcum and adjacent parts of the intestine, may throw some light upon the question of these pericolic membranes.

Through the courtesy of my colleague, Prof. Ferris, I have been able to dissect a series of human embryos and two infants at term and have found conditions which show clearly that these veils are embryonic and normal structures and are not due to the organization of an inflammatory deposit or series of mild infections originating from a chronic colitis.

In the first preparation, an embryo 15½ cm. long, nape-breech measurement, the cæcum (Fig. 5) is still undescended, but the fusion between it and the parietal peritoneum has occurred. Fine veil-like attachments are present, running from the parietal peritoneum just beneath the liver and over the kidney onto the ventral aspect of the cæcum, where they are lost on the mesocæcum. This is an important stage in the development of these pericolic membranes for it represents an excessive degree of fusion of the rotated cæcum with the parietal peritoneum. The usual attachments between the visceral and parietal layers at this point are confined to the posterior aspects of the cæcum and the adjacent portion of the parietal layer. In this case, the appendix lies free in the ileocæcal angle and the terminal ileum is provided with a free mesentery, the posterior leaf of which shows no fusion with the peritoneum.

In an embryo 22 cm. long, nape-breech measurement (Fig. 6), partial descent has occurred. Like the preceding specimen, there are certain atypical and variable features to the attachments between the cæcum and parietal peritoneum. The fusion is most marked at the site of the future hepatic flexure and along the partly formed ascending colon, where the very delicate adhesions marking the fusion of the two layers extend from the parietal peritoneum onto the lateral and ventral surfaces of the colon. The caput cæci is free, but the appendix, caught in these new attchments, shows the effect of the partial descent by being drawn up and kinked along the ventral aspect of the colon with its tip free. It is important to observe that these new-formed attachments which run transverse to the long axis of the colon in the preceding stage, are now drawn partly downwards and are somewhat thinned by the descending cæcum. An effort to lift the terminal ileum reveals that it, too, has partaken in the process of fusion in having the posterior leaf of its mesentery and the posterior aspect of the intestine itself united to the parietal peritoneum by fine, delicate attachments similar to those joining the colon and peritoneum. This is important to bear in mind for, as will be shown later, it represents in its simplest embryonic form a Lane's band.

In an infant at term (Fig. 7), the ordinary conditions found in adult life are present so far as the topography of the cæcum and colon is concerned. Descent has occurred and the omentum is attached to the transverse colon some distance from the hepatic flexure, but a thinned-out portion of the omentum extends over the ventral aspect of the colon as far as the hepatic flexure. Along the lateral margin of the ascending colon, extending from the adjacent portion of the parietal peritoneum and having all of the pericolic veils, are loose membrane-like attachments, the direction of which is now downwards, marking the course of the descended cæcum. The terminal ileum is perfectly free with a mobile mesentery and the appendix is in no way involved in the process of fusion.

Another variation in the usual form of fusion is shown by an embryo 24 cm. long, nape-breech measurement (Fig. 8), where the cæcum is still undescended but is fused posteriorly to the parietal peritoneum over the kidney which can be seen just below the liver and above the cæcum. In this case, no attachments in the form of embryonic membranes extend over the ventral aspect of the colon or cæcum. The appendix, however, is involved in the process of fusion and is attached to the peritoneum just over the kidney, where it shows the effect of the beginning descent in being drawn up and kinked. As is the case in Fig. 6, the tip of the appendix is free, a condition most frequently found in adult life when the appendix is covered by these pericolic membranes.

From a study of these three specimens, it is perfectly clear that unless we accept the unproven theory of fœtal peritonitis, these stages indicate the evolution of the adult pericolic membranes of the commoner type, such as are shown in Figs, 1, 4, 10, and 13, which represent simply a more extensive form of the normal connections between the rotated intestine and the posterior portion of the parietal peritoneum. Usually the fusion takes place only in the approximated portions of the peritoneum and is probably due to some specific chemiotactic action, inasmuch as other parts of the peritoneum at these stages of embryonic life do not participate in the process. At times, however, the fusion is excessive and attachments are formed with the cæcum in the subhepatic position that extend over onto the lateral and ventral aspects of the cæcum and embryonic colon. Given these attachments, the subsequent descent draws them out into the thin veil-like structures that have been described as membranous pericolitis. Both the veils and the parallel vessels in them indicate, as it were, the path of the descent. This process can be appreciated even more readily by reference to the accompanying schema, where the change in position of the cæcum involved in its descent would draw out these fine embryonic adhesions into the form of a veil.

In the series of embryos studied, another infant at term (Fig. 9) throws some light upon the etiology of those veils of the third type which are continuous with the omentum. In this specimen, the following relationships of the cæcum, colon and omentum may be observed: the omentum, with its usual attachment to the transverse colon, extends lateralwards over the cæcum and is attached to the parietal peritoneum adjacent to it. The appendix is free and of the conical infantile type. The fusion between the posterior aspect of the

cæcum and parietal peritoneum has taken place. It must be perfectly obvious that subsequent descent of a cæcum with such omental attachments must give rise (in adult life) to the form of veil shown in Fig. 3, where it extends from the parietal peritoneum over the colon and is continuous with the omentum along its median border. The development of this type of veil may be more readily appreciated from the schema shown in Fig. B, where the superimposed drawings of the earlier and later stages indicate how descent draws out the variable embryonic omental attachments of the cæcum into a pericolic membrane.

These preparations are taken from a relatively small series of embryos, which only serves to emphasize the frequency with which these veils may occur. They naturally vary a great deal in their distribution and extent, but all of those found about the cæcum and ascending colon develop in the manner just described. Surgeons will recognize in these cases where the appendix is involved in the process of fusion, types of appendices which, in adult life, have hitherto been looked upon as resulting from chronic adhesive appendicitis, but which are, in reality, organs that are covered by an embryonic

Fig. A.

Fig. B.

Fig. A.—The black portion of the figure represents the cæcum in its subhepatic position after rotation. The heavy lines the attachments to the parietal peritoneum such as are shown in Fig. 5. It is perfectly clear that subsequent descent would draw out these fine attachments into the form of a veil indicated by the lighter lines.

Fig. B.—The black portion of the figure represents the cæcum in the subhepatic position, with the omentum attached to it and the parietal peritoneum indicated by the heavy black lines. Descent draws out and thins these portions of the omentum into the form of a veil which is continuous with the parietal peritoneum on the one hand and the omentum on the other, as is indicated by the lighter lines.

membrane and not infrequently drawn up and kinked during the descent of the cæcum. In such cases, the cæcum and colon may be free or more frequently involved in the smaller second type of veil. To recapitulate, it will be clearly seen from a study of these specimens, that, after the rotation of the gut, the cæcum becomes attached to the peritoneum of the posterior abdominal wall just under the liver and over the kidney. The precise nature of these secondary attachments has not been worked out by embryologists. In some instances, they are more extensive than in others and may extend out over the surface of the cæcum or ascending colon and, with the subsequent descent, these new-formed connections between the visceral and parietal peritoneum are drawn out in the form of a thin veil, carrying with them their blood-vessels, which take a long unbranching course from their origin on the parietal peritoneum downwards and forwards onto the cæcum or colon, where they communicate with those of the intestinal wall. These secondary unions between the two layers of the peritoneum usually spare the cæcum and extend onto the colon, which give rise to the commoner form of veil (Fig. 1). Occasionally, the cæcum and even the proximal portion of the appendix or, still more rarely, the entire appendix is covered. In such cases, we have the extensive veils which embrace the entire first portion of the large intestine with the appendix drawn up in the process of descent (Fig. 10). In still other instances, the attachments are confined to the region of the cæcum and appendix and thus we have the formation of the veil which simply covers the caput cæci (Fig. 2) with the usual posterior attachments extending up behind the ascending colon.

As there are variations in the form of the secondary attachments between the colon and the peritoneum, so also does the extent of the fusion between the part of the posterior mesogastrium which gives rise to the omentum vary within very considerable limits. Sometimes, the embryonic omentum reaches out lateralwards and fuses with the cæcum before its descent and not uncommonly extends onto the parietal peritoneum. When such a secondary fusion takes place, the cæcum, in its descent drags down the omentum with it and gives rise to that form of veil (Fig. 3) where it is continuous with the omentum along the medial aspect of the large bowel.

Not only from the appearance of the veils themselves, but from the conditions shown in the human embryos and infants just described, it is clear that these pericolic membranes are not the products of inflammation, nor are they the residue of repeated attacks of colitis. It is likewise clear that the view which regards them as the result of a burrowing of the cæcum behind the parietal peritoneum cannot obtain. They represent simply either more marked attachments of the large intestine to the posterior abdominal wall or else, in some cases, a more extensive fusion of the omentum to the colon, which is dragged down with the descent of the cæcum and gives it an attachment on the ascending colon continuous with an embryonic membrane.

Symptoms.

The question of the greatest importance from a clinical standpoint is whether or not these embryonic membranes are ever responsible for symptoms. While, in the great majority of cases, they are not the cause of any trouble to their possessor, I think there is no question, however, that in certain instances, either alone or in combination with other circumstances, they may give rise to symptoms of a very definite nature which are not infrequently either confounded with or associated with chronic appendicitis. When the veils are extensive and badly placed from a mechanical point of view, they may cause obstruction, especially if any degree of ptosis is present. It is not impossible that they may become somewhat thickened as a result of chronic colitis. This is indicated in the denser strands of connective tissue in some veils,

associated with distention of the cæcum, exaggerated or irregular sacculation of the colon, and the unrolling of the intestine after such veils are incised. Veils continuous with the omentum may, if the transverse colon is redundant, hold the hepatic flexure in acute angulation. Patients with such membranes may suffer, not only from the mechanical interference with the intestinal circulation, but may have sensations of pain and distress on the right side more or less exacerbating in character and often show on palpation distinct tenderness over the ascending colon well above the appendix and cæcum. In three instances, my cases have shown points of tenderness over the cæcum or in the pelvis on the right side, as well as a marked reaction high up in the flank. In these cases, the chronically inflamed appendix was found hanging over the brim of the pelvis and a well marked veil on the ascending colon. One instance was in a child of 12, the second in a youth of 18, and the third in a very well nourished woman of 29. In these cases, there was no ptosis; no question of involvement of the kidney and ureter, and no chronic colitis. None of the patients was neurasthenic. There could be no other interpretation of the symptoms and findings at operation, except that the flank pain was due to the constriction of the embryonic membranes. Incision of the veils relieved all three of the cases. That such symptoms may follow their presence is even better shown in the instances reported by Jackson and Connell in which simple appendectomy gave no relief, but where reoperation and removal of the veils accomplished the desired result. A patient upon whom I operated some time ago emphasizes this occasional association of the membranes with symptoms. For years she had suffered with pains of varying intensity on the right side over the cæcum and ascending colon. She was operated upon in the fifth month of a pregnancy complicated by multiple myomata, one of which was strangulated. After the hysterectomy and appendectomy, her condition did not warrant any further interference, so the well marked embryonic veil covering the cæcum and ascending colon was left undisturbed. The appendectomy has had no influence whatever upon the pain on the right side although in other respects she is quite well.

Embryonic veils which embrace the appendix usually kink it and probably are responsible for many of the cases of chronic appendicitis in which they occur. Veils of this type have usually been interpreted as adhesions about the appendix resulting from previous infections. Most operators have frequently been surprised to find a bound-down, kinked and adherent appendix in a case that has never had an acute attack. In such instances the adhesions are usually these embryonic membranes. I have seen two cases where the appendix was constricted and partly obliterated at the point of attachment of a veil, which led to an acute infection of the appendix from the interference of its drainage into the large intestine.

We have come to suspect the presence of these veils as the cause of symptoms in these cases which complain of pain in the right side, usually most marked in the flank and right lower quadrant, which have never had an acute attack of appendicitis and in which the possibility of renal and ureteral involvement can be ruled out. Most frequently, such patients complain of chronic obstruction which usually intensifies their symptoms.

Treatment.

Several suggestions have already been made for the treatment of these pericolic membranes. By some, the veils have been stripped off and the colon denuded of some of its peritoneum in consequence. Another suggestion has been to dissect off the veil and use it as a strand to support the cæcum from sinking into the pelvis. Lately we have simply incised the membrane along the lateral border of the colon and allowed the intestine to unroll and become free. In our first few cases, when we were under the impression that the membrane was inflammatory, we stripped the veil, but later confined any operative interference with it to those cases only where we felt that it was responsible for pain and discomfort or else was offering some mechanical obstruction to the intestinal current. In any case, incision is all that is indicated, for any obstruction can be relieved in this way. Stripping leaves a denuded surface which may lead to the formation of adhesions or cause, in healing, the formation of a new inflammatory membrane which might be worse than the embryonic veil. In those cases where the membrane is continuous with the omentum, the operator may free the omentum by incision and ligation of the bleeding points. By far the best treatment in the majority of cases will be to let them alone, for it must not be forgotten that these are normal embryonic structures of quite common occurrence and they should not be interfered with in the absence of definite indications for their incision or removal. Furthermore, it is especially important to be cautious in attaching any pathological significance to structures which may be simply more or less uncommon anatomical variations of the normal attachments of the colon.

Lane's Band and Kink.

In recent years, everyone has become familiar with the work of Arbuthnot Lane on chronic constipation and the careful study he has made of the mechanical factors that interfere with the fecal current in the intestine. Various aspects of this problem have been discussed by Lane in an interesting series of papers. The great frequency of chronic appendicitis and the association of the disease with chronic obstruction have centered interest more or less upon the band and kink first described by Lane in the terminal portion of the ileum. This condition can best be explained in Lane's own words: "There develops on the under surface of the mesentery of the last few inches of the small intestine a new band, which at first forms part of the under surface of the mesentery. Later it forms a ligament distinct from the mesentery. This ligament contracts and deforms the ileum, producing a kink or obstruction of this portion of the intestine, especially in the erect posture of the trunk. In consequence of this kink, the small intestine becomes very much dilated and this dilatation may extend up as far as the pylorus. The symptoms produced

by this obstruction are superficially very much like those of appendicitis and, in consequence, a large number of normal appendices have been removed to bring about a cure of symptoms resulting from this obstruction, needless to say, without any particular benefit to the patient." Lane, himself, ascribes the formation of the bands to ptosis of the cæcum, a tendency which crystallizes the lines of strain into peritoneal adhesions resulting in a kinking of the gut and a rolling of the intestine on itself. Since the appearance of Lane's papers, a number of observers have reported cases and offered suggestions as to the possible etiology of the condition. Martin, who has studied the problem, reports the results of his investigations as follows: "From a somewhat careful observation of a limited number of cases, I have concluded that the kinking of the ileum within four inches of its cæcum attachment instead of elsewhere, is due to the fact that the ileum at its termination in the large bowel possesses an extremely short mesentery, viz., from one to two inches. Given this comparatively fixed portion of the compressible tube, there are two factors which lead to its distortion: (a) A too movable and displaced large bowel, and (b) an abnormal disposition of the remaining portion of the small bowel or other viscera." Martin does not think that chronic inflammation of either the appendix or adjacent viscera has any particular influence on the formation of these bands. Charles Mayo, also a contributor to this subject, states that: "During the past two years we have observed many cases in which there was a definite kink in the ileum within a few inches of its termination. The ileum was rolled over and fixed upon its mesentery, evidently a condition of inflammatory origin. Sometimes these adhesions, with resulting bands of peritoneum causing a kink, appear to be of congenital development because the condition has been reported in children without evidence of local inflammatory cause. It has been observed that when adhesions were present, or when the peritoneal bands were greatly thickened, the appendix also showed chronic inflammation which was apparently the source of the peritoneal thickening. The relief afforded by freeing the bowel of the adhesions indicates that this is undoubtedly a condition which has much to do with the ill health of the individual, even though the greater number of symptoms were not local but reflex in character, acting upon the stomach and intestines."

In the past two years I have met with 11 cases of Lane's band of which 5 had, at the same time, embryonic veils upon either the cæcum or ascending colon. Of the 11 cases, 8 had marked kinks and the remainder were slight and not associated with any evident obstruction to the lumen of the small intestine. In the gross characters of the bands, none of them looked like acquired adhesions. Some were thin and delicate like the pericolic membranes, while others were thicker and firmer although not of the same character as acquired inflammatory adhesions. On two there were secondary deposits, inflammatory in nature, resulting from attacks of appendicitis. For the most part they extend from the free border of the intestine opposite the mesenteric attachment onto the posterior leaf of the mesentery and thence, if that is short, to the parietal peritoneum over the psoas muscle along the brim of the true pelvis. The discovery of a marked band at autopsy in an infant 11 months old, where neither the illness nor the cause of death was in any way associated with the intestine, forced the conclusion already reached by Mayo that some of these cases were certainly congenital. During the study of the embryos with reference to the attachments of the cæcum and large intestine, a careful inspection of the terminal portion of the ileum was also made to determine just to what extent these bands were present before birth and to see if any rational explanation of their formation could be found.

In this part of the alimentary tract, as in the first portion of the large intestine, there is a great deal of individual variation in both the relations and the attachments of the terminal portion of the ileum. In all of the embryos, except two, the terminal ileum possessed a free mesentery, but it varied considerably in length. In some cases it was short, while in others it was long and free. In almost all cases, however, on the posterior leaf of the mesentery, there was a point of reflection onto the parietal peritoneum over the psoas muscle or just over the brim of the pelvis, the exact point depending on the age of the embryo and the degree of descent that was present. This is well shown in one of the infants at term (Fig. 9), where the mesentery is free and long, but where the cæcum is not yet descended. On lifting the ileum to bring the posterior leaf in view, a distinct fold running from a point near the psoas up onto the posterior leaf is clearly seen. This is the condition which one finds in almost all adults, whether the mesentery is either short or long. In the embryo (Fig. 6) 22 cm. long with a partially descended cæcum, the process of fusion between the cæcum, colon and the parietal peritoneum had apparently involved the terminal part of the ileum as well, so that we have a well marked Lane's band at this stage of fœtal life. As the free part of the ileum is lifted, the delicate attachments that connect the portion adjacent to the ileocæcal valve with the parietal peritoneum are shown. In this instance, union has taken place well down onto the intestine. In a second case, of an embryo (Fig. 8) 24 cm. long, where the cæcum is still undescended, a similar state of affairs is observed except that the posterior leaf is a trifle freer than in the preceding instance. The band was observed for a third time in the case of the 11 months infant noted above (Fig. 12) who died the day after admission to the hospital from cachexia, due to an ovarian teratoma. In this case, the cæcum was undescended, the appendix infantile, and there was a well marked embryonic band uniting the terminal ileum with the posterior peritoneum, almost obliterating the posterior leaf of its mesentery.

In these three instances, occurring in embryonic life and just after birth, we have not only a Lane's band present, but also the explanation of its formation. The band is associated with the fusion that takes place between the rotated intestine and the parietal peritoneum. In all instances, it may not be the result of a direct fusion, for when an attachment takes place in embryos with a short mesentery between the posterior leaf of the mesentery and the parietal peritoneum, while the

ileocæcal junction is still in the subhepatic position, the subsequent descent might tend, owing to the point of fixation, to shorten the posterior leaf of the mesentery and to roll the intestine on itself.

It is probable that this condition is much more frequent than we suspect and that there are many cases where the possession of such a band is not the slightest inconvenience to its possessor. On the other hand there is no question that the presence of these bands may offer serious obstruction to the intestinal current, especially if it is associated with hyperdescent of the cæcum or a condition of acquired ptosis. I think it would be well for surgeons to recall that all cases of pelvic cæcum are not ptotic, for, as Smith has shown in his study of the conditions in 1000 infants, hyperdescent takes place in 10% of the cases and the cæcum lies in the true pelvis. Now, in patients with acquired ptosis or those in whom the hyperdescent is excessive, or those in whom embryonic membranes lie over the cæcum or ascending colon in such a way as to offer obstruction, the presence of these bands may take on a definite pathological significance and become a potent source of delay in the passage of the intestinal contents, not

Fig. C.—Diagram A shows the terminal ileum with its mesentery cut in cross-section. The fine lines represent the embryonic Lane's band. Descent with the cæcum, indicated by the arrow, would tend, owing to the fixation, to roll the intestine on itself and possibly kink it (B).

only in a diminution of the lumen of the gut itself, but in the formation of a definite kink of the ileum as Lane has pointed out.

Symptoms.

The symptomatology in our cases has varied from none attributable to the band itself, but where the disease was chiefly in the appendix, to marked cases with definite obstruction. The differentiation between the symptoms of an obstructing band and chronic appendicitis is often difficult or impossible, as Mayo has pointed out, when the two conditions occur in the same patient.

The symptoms that may be referred to the band are chiefly those of obstruction which is usually chronic. The patients suffer from constipation, the bowels often moving only with the aid of catharsis. There are not infrequently attacks of colic which may be severe enough to simulate an early acute obstruction. In fact, two of my most marked cases had periods of acute obstruction lasting several days. One was operated on for the obstruction. The more usual complaint is one of continual distress or discomfort on the right side low down or about the umbilicus, with frequent severe attacks of pain and colic which are aggravated by the periods of constipation. There are also cases where the referred symptoms predominate and the patient complains chiefly of the distention and eructations of gas. These usually are worse some time after meals. They are, however, not like the characteristic hunger pains of duodenal ulcer. The frequent association of embryonic bands upon the cæcum or colon with kinked or chronically inflamed appendices makes a definite diagnosis of the band alone improbable in very many cases. The usual points of tenderness on the right side along the terminal ileum is not, as a rule, capable of being dissociated from the tenderness of the appendix.

Treatment.

The treatment that has been followed by all surgeons consists in an incision of the band along the mesenteric border of the intestine, allowing the gut to unroll and the kink to straighten out. This can be accomplished with the point of a sharp knife or by passing a pair of anatomical forceps under the band and incising between the blades. It is remarkable how the intestine will unroll and the kink disappear after the release of the constricting action of the band. Martin keeps his patients in the Trendelenburg position after the operation to prevent the reformation of the band by lengthening the posterior leaf of the mesentery and Mayo accomplishes the same result in some patients by smearing the denuded part of the peritoneum with sterile vaseline. We have counted on the usual post-operative distention of the gut to keep the released intestine from either kinking again or allowing obstructive adhesions to form over the area denuded of peritoneum.

Embryonic Bands on the Gall-bladder.

Another type of embryonic band which is familiar to anatomists and embryologists, but to which no one, so far as I am aware, has ascribed a definite symptomatology, is a small band like a mesentery which extends from the gall-bladder onto the transverse colon to become continuous with the omentum. It is thin, relatively avascular, and contains but little fat. In some cases the fundus is free and in others the mesentery extends well up to the tip of the organ. Attention has again been called to this omental mesentery of the gall-bladder recently by Rubin in his interesting paper on the functions of the omentum. He states that he has only observed the condition in children and infants where pathological changes are out of the question. Recently, I found in the same infant (who had died of an intercurrent disease) an example of this variation of the omental attachment, with a Lane's band and undescended cæcum. It was apparent that this was simply an embryological band such as has been frequently seen and owed its origin to the fundus catching up a portion of the omentum as it grew out from the common duct. A few weeks later, a patient entered the hospital with the following rather remarkable history:

The patient, Miss D., is an extremely intelligent young woman of 20. About three years ago she fell and received a blow on the abdomen just above the hip. Since that time she has had a constant pain on the right side which becomes very sharp and radiates to the right shoulder on any extra exertion, especially like jarring or twisting the right side. Indigestion or accumulation of gas in the intestines increases the pain in the side. On taking a deep breath a sharp pain is noticed in the right hypochondrium (patient points to the gall-bladder region). Recently she has much discomfort in the epigastrium, especially after eating, when she feels as though her stomach is distended with gas. Her bowels are more constipated, a condition which dates practically from the onset of the present illness. She has no nausea or vomiting, the attacks are not associated with fever or feelings of general malaise. The general physical examination is negative. There is no tenderness or fixation of the spine; sacro-iliac and hip joints negative. The abdomen is soft and everywhere tympanitic. Stomach tympany not increased. There is distinct tenderness on deep palpation over the gall-bladder. Along the right flank there is also a slight response to deep palpation. Over the region of the cæcum at Lantz's point there is an area of tenderness with a sharp muscle spasm on deep palpation. Rectal examination negative. The urine is clear and the kidneys are neither felt nor tender.

At the operation, a well-marked embryonic veil was found extending down from the parietal peritoneum near the hepatic flexure over onto the ascending colon and cæcum. The membrane embraced the proximal part of the appendix. The appendix was removed and the veil incised. An exploration of the gall-bladder showed an embryonic band like a mesentery extending from the cystic duct up to the fundus over onto the transverse colon, where it was continuous with the omentum. Its character was exactly like that of the one found in the infant. This band was incised so that the gall-bladder and colon were liberated. There was no question of any inflammatory reaction about the gall-bladder. It had a smooth and glistening peritoneum, was not thickened, and its contents could be squeezed by gentle pressure into the duodenum. It contained no stones.

This case presents many interesting features. The patient had carried the pericolic membrane and the mesentery of the gall-bladder from birth without symptoms until the time of her fall, when the supports of the large intestine were probably weakened so that the band about the colon began to interfere with its function and a certain amount of traction was exerted on the gall-bladder by its omental mesentery when the patient took a deep breath or indulged in extra or unusual exertion. On such occasions the characteristic pain of the gall-bladder radiating to the shoulder would occur. Liberation of both bands relieved her of the symptoms completely. The patient had three points of tenderness, namely, the gall-bladder, the ascending colon and the appendix. Bands on the two former organs were responsible for pain and tenderness, while the chronic inflammation of the appendix was brought about by the extension of the veil over its proximal portion.

The conditions presented by these patients with embryological bands all simulate to a greater or less extent conditions that are familiar to us in chronic appendicitis. A differentiation between them is often difficult, and sometimes impossible, when the two conditions occur simultaneously in the same patient. The point to be learned is that a group diagnosis of chronic appendicitis will leave many unbenefited patients if the therapy is limited to an appendectomy. The day of inch incisions for appendicitis is over and every case of chronic appendicitis should have an incision large enough to afford an opportunity to explore the terminal ileum and ascending colon. Such an incision heals as strongly as a small one if it is properly closed. A patient who takes an anæsthetic is entitled to have a visual exploration of the accessible portion of the abdomen made to supplement the less accurate clinical and pre-operative methods of diagnosis and investigation.

The study also emphasizes that we should ascribe pathological significance to normal, but variable, structures with great hesitation. It is also essential to be familiar with the type variations of the different viscera. Difficulties in the interpretation of pathological conditions thus become simpler and the attempt to restore normal relationships easier.

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EXPLANATION OF PLATES.

Fig. 1.—Common type of membrane extending from the parietal peritoneum near the hepatic flexure downwards over onto the ventral aspect of the ascending colon. Caput cæci and appendix free.

Fig. 2.—Embryonic membrane extending from the parietal peritoneum over onto the caput cæci, involving the proximal portion of the appendix, which is kinked.

Fig. 3.—Embryonic membrane extending from the parietal peritoneum near the hepatic flexure onto the ascending colon and cæcum. With the exception of the tip, the entire appendix is covered by the veil. The membrane extends across the colon and is continuous with the omentum.

Fig. 4.—Marked veil over the colon, cæcum, and proximal portion of the appendix, which is kinked and drawn upwards during descent. Note the thickened strands of connective tissue in the membrane causing irregular sacculation of the cæcum and colon. A well-marked Lane's band is present.

Fig. 5.—Human embryo 15½ cm. long. Cæcum undescended. Secondary fusion between the parietal peritoneum and cæcum. These secondary attachments between the parietal peritoneum and the embryonic intestine extend over the cæcum and colon to the mesocæcum and mesocolon. Descent of the cæcum in a case like this leads to the formation of an embryonic membrane such as is shown in Fig. 1. The caput cæci, appendix, and terminal ileum are free.

Fig. 6.—Human embryo 22 cm. long. Cæcum partly descended. Embryonic membrane extending over the appendix and ascending colon. Elevation of the terminal ileum reveals the fusion between the posterior leaf of the mesentery and the ileum itself in the form of an embryonic Lane's band. With an attachment like this, the ileum may roll on itself during descent.

Fig. 7.—Infant at term. Cæcum descended. Well-marked embryonic membrane extending from the parietal peritoneum over the ascending colon and cæcum. Such a membrane results from

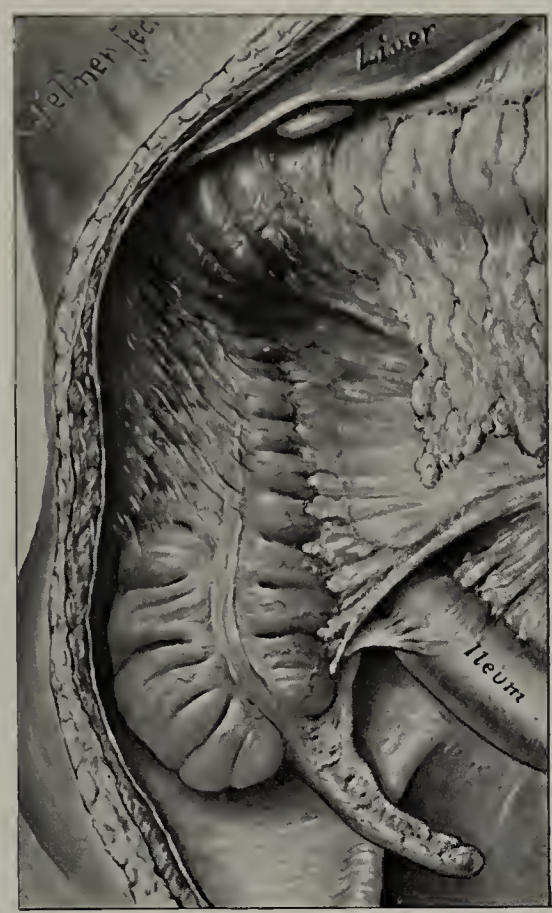

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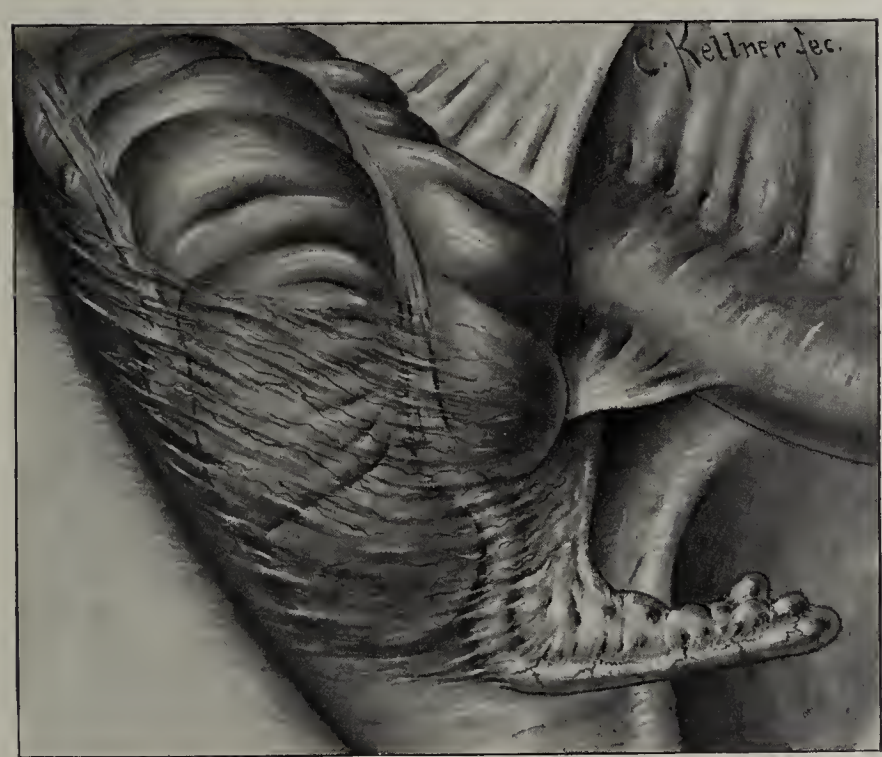
Fig. 3.



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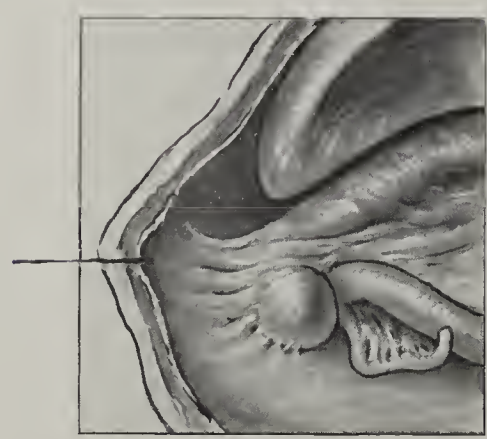

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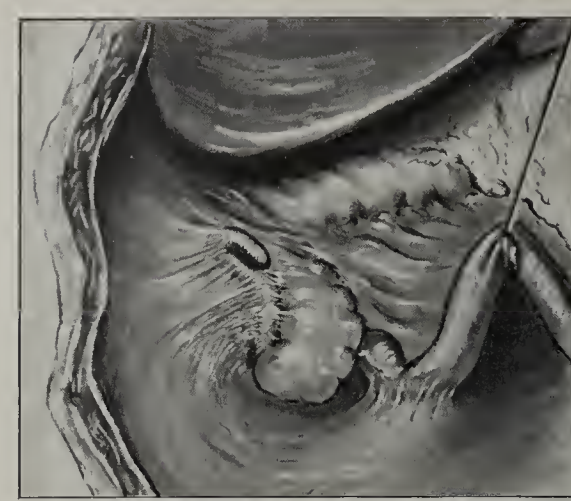

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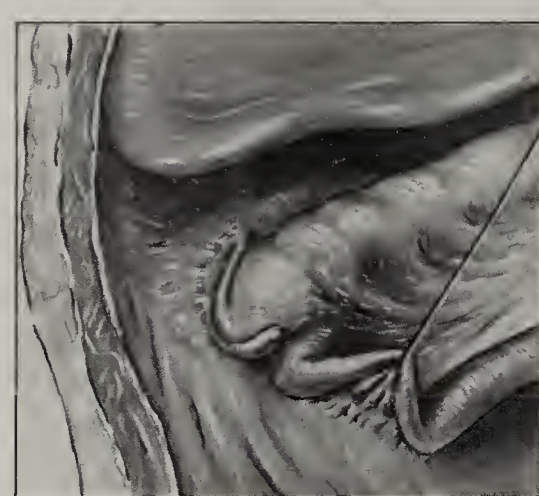

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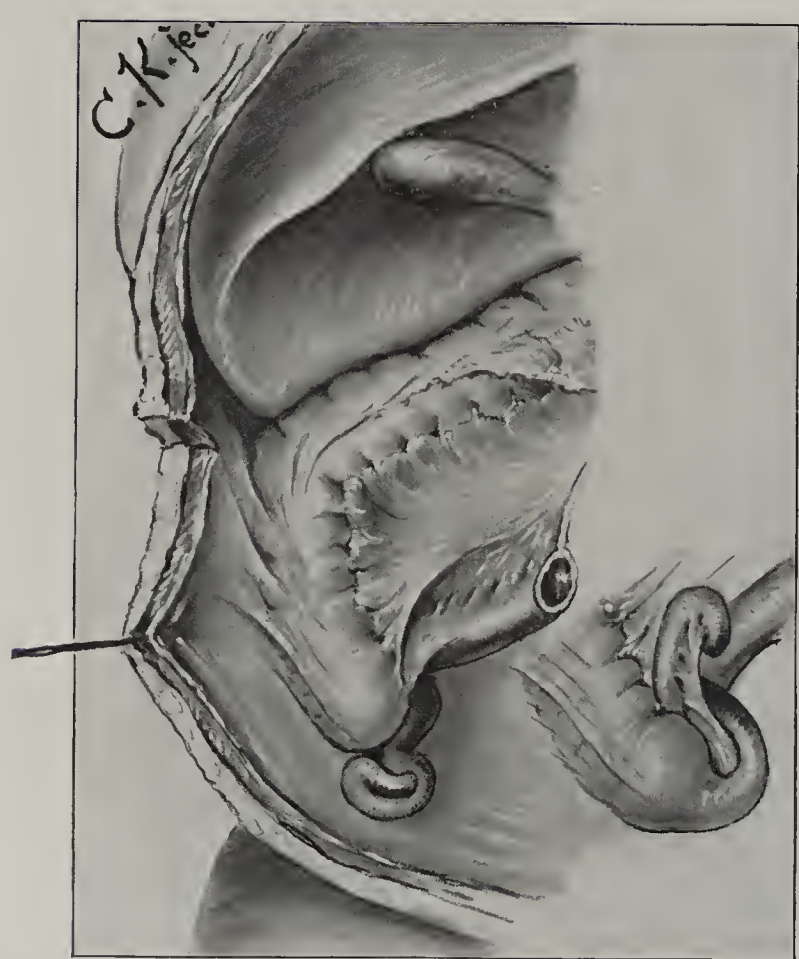

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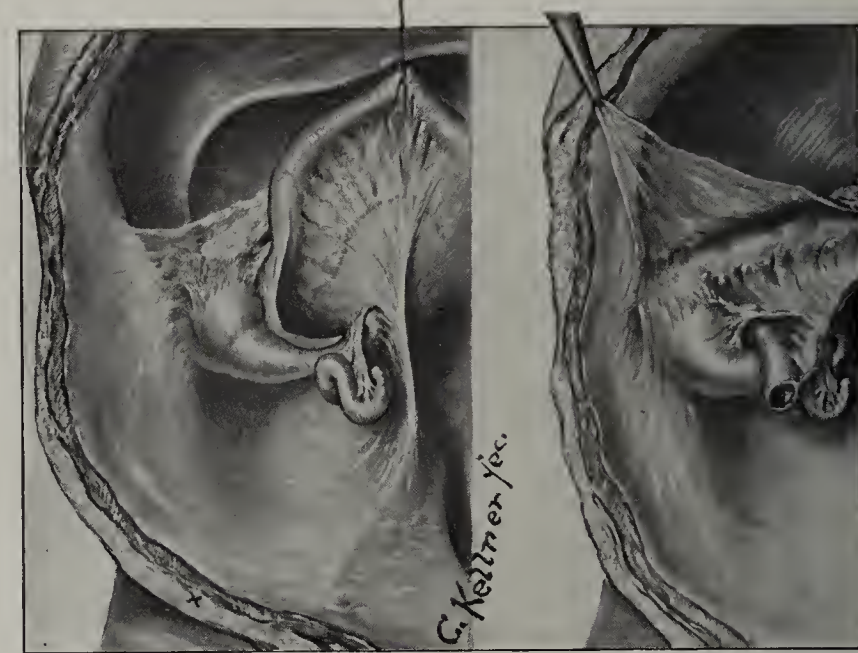

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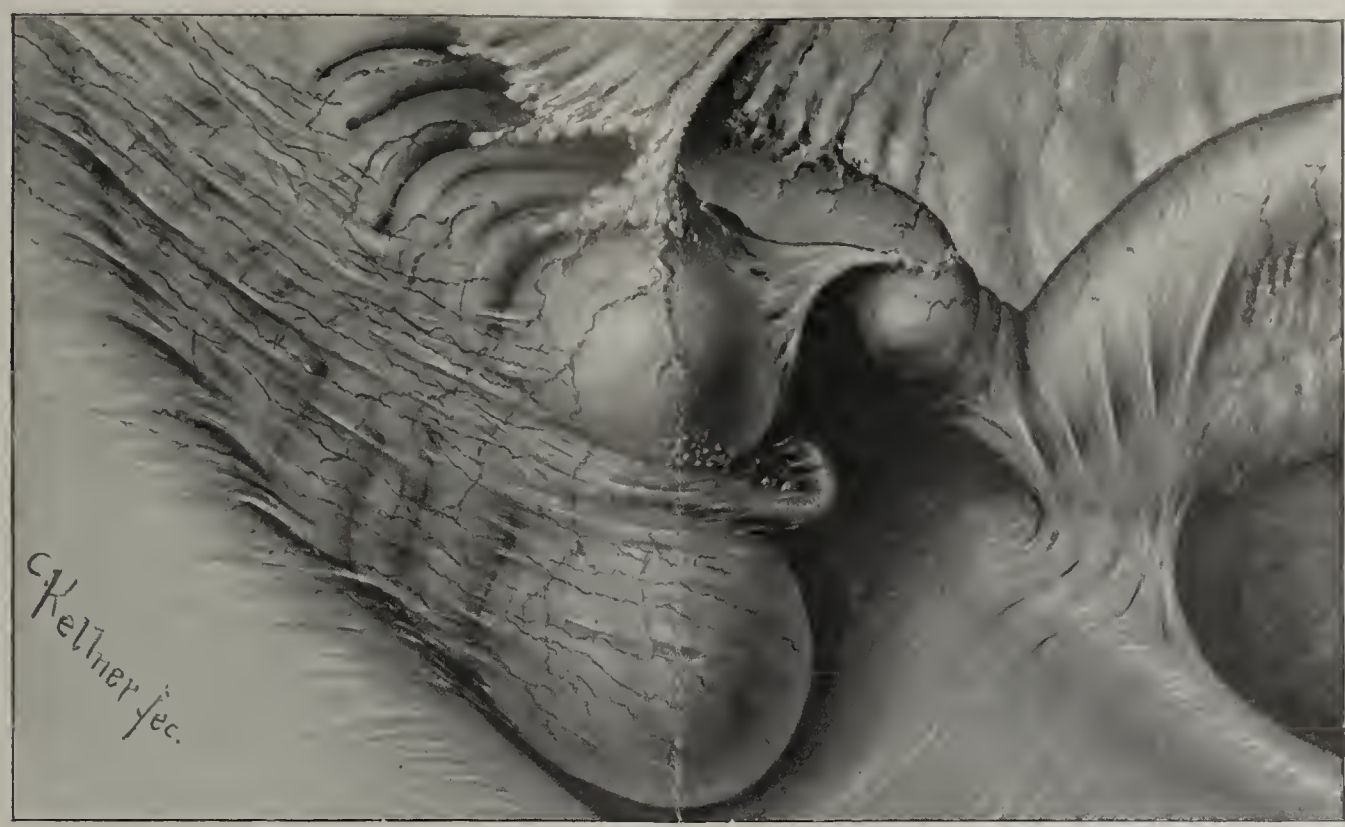

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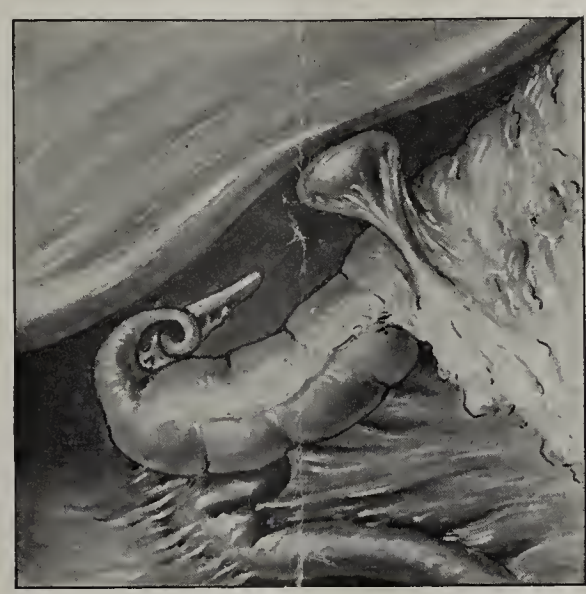
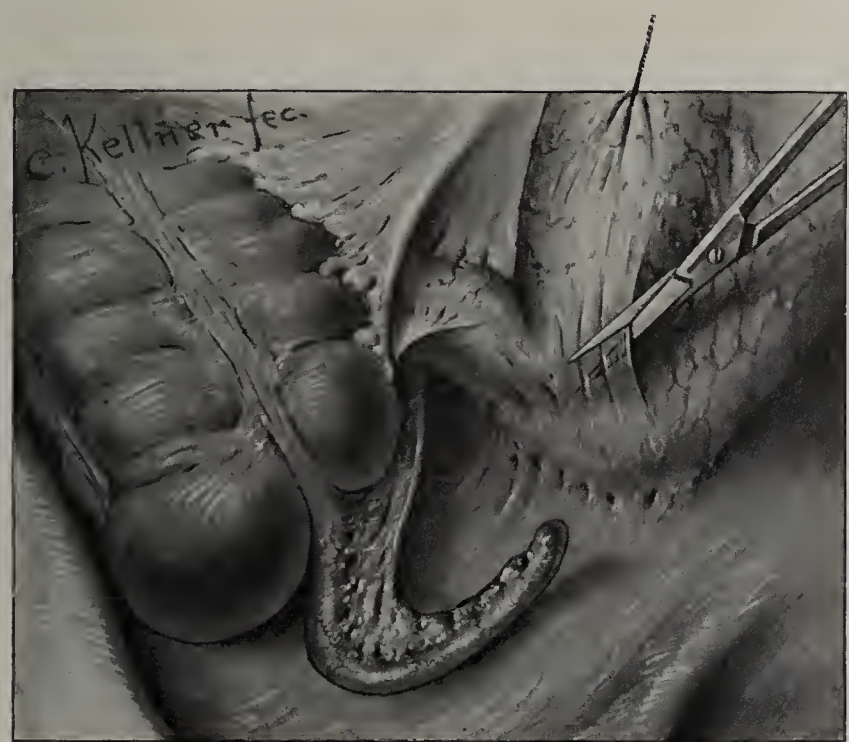


Fig. 12.



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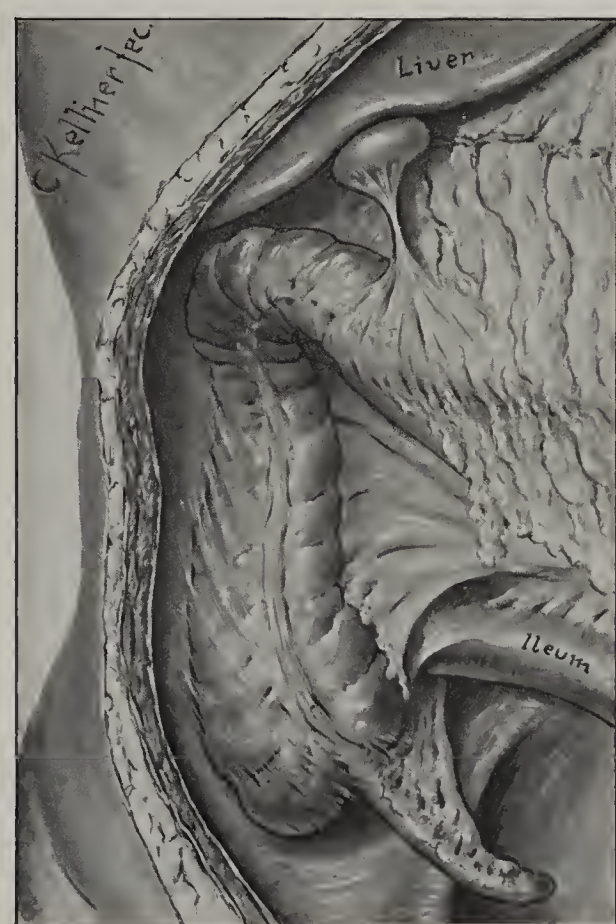

Fig. 13.

the descent of the cæcum when the attachments in earlier embryonic life are like those shown in Fig. 5. This represents the embryonic form of the membrane illustrated in Fig. 1. The appendix and terminal ileum are free.

Fig. 8.—Human embryo 24 cm. long. Cæcum undescended. Cæcum fused to the parietal peritoneum, the process involving the appendix, which is kinked. The terminal ileum shows a partial fusion to the parietal peritoneum forming an embryonic Lane's band. It is this type of fusion when it extends onto the caput cæci that gives rise to the type of veil shown in Fig. 2.

Fig. 9.—Infant at term. Cæcum undescended. Extensive attachment of the omentum over the cæcum and ascending colon to the parietal peritoneum. Subsequent descent of the cæcum with omental attachments of this nature gives rise to the form of veil shown in Fig. 3. Elevation of the ileum shows the reflexion of the parietal peritoneum onto the posterior leaf of the mesentery. This is the common type seen in adult life.

Fig. 10.—Marked Lane's band showing the kink and rolling of the intestine resulting from embryonic fusions between the terminal ileum and parietal peritoneum such as are shown in Figs. 7 and 8. There is also a well-marked embryonic membrane extending over the ascending colon and cæcum involving the appendix, which is drawn up behind the cæcum during descent.

Fig. 11.—Marked Lane's band and kink causing obstruction and dilatation of the small intestine.

Fig. 12.—Infant 11 months old. Cæcum undescended. Lane's band. Omental mesentery to the gall-bladder.

Fig. 13.—Omental mesentery to the gall-bladder causing symptoms. Embryonic membrane over colon, cæcum, and proximal portion of the appendix.

REFLEX ALBUMINURIA.

RENAL ALBUMINURIA SECONDARY TO IRRITATION OF THE URINARY BLADDER.

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(From the Hunterian Laboratory of Experimental Pathology, The Johns Hopkins University.)

Studies in metabolism conducted upon dogs, in which the urine may be obtained by means of a catheter or, perhaps, through a cannula sewn into the bladder, are often complicated by the appearance of more or less albumin in the urine. At first thought, one might assume that this albumin was derived from the irritated bladder mucosa, but the amount is considerable at times, and we shall attempt to show that this albumin in great part is derived from the kidneys. It seems that this is a true renal albuminuria and that some nervous reflex must be responsible for it—that transient or continuous irritation or inflammation of the bladder mucosa can cause a true reflex response on the part of the kidney. The path of this reflex will be interesting to investigate, as well as the action of various other stimuli upon the bladder or organs in the immediate neighborhood supplied by the same plexus.

In some cases this reflex is so prompt and noticeable as to remove all doubt in one's mind concerning the possibility of ascending infection along the ureters. Whether the arc is completed by the sympathetic chain or not is still to be determined, but it is an interesting observation that the renal epithelium can respond so actively to certain localized outside stimuli.

It will be rather easy to approach this problem in the case of human beings, especially in females. It is not difficult to imagine some long-standing source of irritation (calculi, tumors or cystitis) which might be associated with an albuminuria of slight or progressive degree. A constant albuminuria will be associated with casts and a certain grade of stagnation of urine in the tubules, which will handicap the kidneys and lead to further injury—a vicious circle with progressive degenerative changes. If this handicap is imposed on kidneys already diseased, it may cause a progressive injury to the renal epithelium and bring about sufficient damage to overwhelm kidneys which may be working close to their maximum capacity.

That the presence of calculi in the ureter or kidney pelvis may cause interesting reflexes is familiar to all, but we have not found any observations upon the point in question—the reflex action of bladder irritation upon the kidney secretion.

Paschkis reports some cases of vesical calculi showing albumin in the urine, and Eastmond reports two cases having renal symptoms with bladder calculi but neglects to say of what nature these symptoms were. Fenwick gives an account of an inflammation at the umbilicus resulting in a reflex cystitis, and calls attention to the difference between the embryological relationship that exists between the umbilical region and the bladder and that between the kidney and bladder. Upon the knowledge of this difference he expresses the opinion that, having an ascending infection and possibilities of obstruction, a bladder calculus has no influence on the functioning of the tract. As opposed to this, Lewis expresses the opinion, based upon observation of his own cases, that a calculus anywhere in the urinary tract will cause albuminuria but makes no further observation bearing on the question under consideration here. Treves reports in brief the case of a Newfoundland dog which died of uræmia and showed at autopsy normal kidneys and a large bladder stone.

Method 1.

Dogs were used in all these experiments and usually fox terrier females, as they were best suited for our purpose. Only in very young dogs was it needful to dilate the vagina, and in no instance was the vagina cut to expose the urethral papilla, which favors bladder infection. Before operation the urine was invariably tested for albumin, and, as a rule, the dogs were rejected which showed existing albuminuria. In our experience an albuminuria of ¼ gm. per litre (Esbach) is not a very infrequent finding in healthy dogs—especially older animals. The animals

were kept the greater part of the time in large cages but were allowed to exercise in the yard at various times.

The foreign bodies introduced into the bladder were various. The common five-cent piece, weight 5 gm., diameter 2 cm.; marbles, which were soaked in acid to remove their smooth coating and filed to further roughen the surface, weight 3.2 gm., diameter 1½ cm.; buttons, the common metal collar button and the familiar enameled bachelor's button with two separate parts which snap together, weight 2.5 gm., diameter 1.7 cm.

All operations were done under surgical ether anæsthesia with aseptic precautions. Only the more complete experiments are cited here, but all our observations were in harmony and we believe that the experiments detailed below are sufficient to make our points clear. Urine was usually obtained by catheter, but when this was not available it was collected under a clean metabolism cage. Dogs with a certain grade of cystitis are apt to urinate very frequently, and it is often difficult to obtain any considerable amount by catheter.

Albumin was detected in the urine by familiar clinical methods. (1) Heller's nitric acid contact test, with urine diluted with equal volumes of distilled water. (2) Heat and dilute acetic acid. (3) Esbach's test, using the reagent modified by Tsuchiya (phosphotungstic acid 1½ gm., concentrated hydrochloric acid 5 cc., and ethyl alcohol to a volume of 100 cc.). In this test the urine was first diluted with equal volumes of distilled water.

In washing out the bladder to obtain urine free from exudate from the bladder mucosa, it was found best to give the dog a large amount of water by stomach tube and await the appearance of a brisk diuresis. When the diuresis was at its height the animal was placed upon a table, a catheter inserted and the bladder washed out repeatedly until the washings gave not the slightest evidence of any albumin. Urine was collected during the next few minutes, and this was looked upon as practically pure renal secretion, for it is difficult to believe that the degree of cystitis usually present could add any appreciable amount of albuminous exudate to the urine during this short time.

The catheterization of the ureter was done usually on the left side, with as little handling of the tissues as possible. A small glass cannula was tied into the cut ureter a few centimeters below the pelvis, the urine collected, and later the kidney was extirpated. Under anæsthesia it is necessary to give normal saline solution intravenously to promote a satisfactory diuresis.

Gross and histological examination of the kidney removed at operation or the entire urinary tract at autopsy was made in every instance. The ureters and pelves were examined with especial care. The tissues were fixed usually in formalin and stained in the routine manner.

Dog B-24.

1-9-'12. Dog, female, fox terrier, weighs 10.7 kilos (23.5 lbs.), in good condition.

Operation: A five-cent piece was introduced into the urinary bladder.

1-13-'12. 71 cc. of urine pipetted from floor after giving animal 300 cc. of water by the stomach tube.

1-16-'12. Animal weighs 10.3 kilos (22¾ lbs.) and is in good condition.

1-25-'12. Animal weighs 9.5 kilos (21 lbs.) and is in good condition.

1-27-'12. Gave 300 cc. of water by stomach tube. Diuretic time about 1 hour and 15 minutes (height of diuresis attained in 1¼ hrs. after giving the water).

1-30-'12. Gave 300 cc. of water by stomach tube. Diuretic time about 1 hour and 30 minutes.

2-1-'12. Animal weighs 9.4 kilos (21¾ lbs.) and is in good condition. Gave 400 cc. of water by stomach tube. Bladder was washed as described above. Could not get urine for test.

2-3-'12. Gave 500 cc. of water by stomach tube. Washed out bladder in usual manner. Collected urine during first 10 minutes of the washing (see table) and again at end of first 20 minutes after washing (see table). Albumin and few casts present.

2-6-'12. Gave 500 cc. of water by stomach tube. Washed out bladder in usual manner and collected urine for the following 15 minutes.

2-8-'12. Animal weighs 9.5 kilos and is in good condition.

2-10-'12. Gave 500 cc. of water by stomach tube. Washed bladder in usual manner and collected urine during the first 15 minutes following washing (see table).

2-13-'12. Gave 500 cc. water by stomach tube at 11 a. m., 700 cc. at 1.15 p. m. and 300 cc. at 2.30 p. m.

Operation: Catheterized left ureter about 3 cm. from pelvis of kidney.

3.45 p. m. 40 cc. of urine from bladder by catheter.

3.50 p. m. Began infusion of sterile salt solution into right femoral vein.

4.10 p. m. 500 cc. salt solution infused.

4.20 p. m. 400 cc. salt solution infused. Urine started and flowed and bladder was catheterized (see table).

5.35 p. m. 1600 cc. salt solution infused (total). Bladder catheterized (see table), and kidney removed.

2-14-'12. Animal died at 5.30 p. m.

Autopsy, 5.40 p. m. Kidneys: Acute congestion, otherwise normal. Ureters: Normal. Bladder: Subacute cystitis. Lungs: Bronchopneumonia and œdema. Other organs normal.

Microscopical sections: Kidney removed at operation. The cortex shows congestion of all the vessels. The stroma everywhere is normal. The epithelium of the convoluted tubules is perfectly normal, and the glomeruli also are normal. The vessels of the pyramids are greatly congested. The epithelium of the collecting tubules shows a moderate grade of fat in fine droplets. Kidney removed at autopsy presents an identical appearance with the other. Bladder: The epithelium is intact. It is considerably thickened, and the papillæ in places are very conspicuous. There is a suggestion of metaplasia of the epithelium in places. The submucosa shows engorged thickened vessels. It is definitely thickened and the tissue is infiltrated with large numbers of mononuclear cells, with occasional polymorphonuclear cells.

Summary, Dog B-24.—A strong female fox terrier was operated upon and a five-cent piece introduced into the urinary bladder. The urine before operation was negative for albumin and casts. For a few days following the operation a large amount of albumin was present in the urine. Albumin was constantly present during the three weeks following the operation after the animal was active and in perfect health, the wound healing per primam. *Casts* were first noted at the end of the third week and were constantly present in small numbers after this. After a space of four weeks the dog was given 500 cc. of water by stomach, and after diuresis was active, the bladder was rinsed out thoroughly and the urine collected during the next 10 minutes. This dilute urine contained considerable *albumin,* and it seemed certain that this albumin must have been derived from the renal and not from the bladder epithelium. A few casts were present. The same procedure a few days later gave identical results. Albumin was present in the dilute urine—¾ gm. to the litre.

At the end of five weeks the dog was operated upon and the left ureter catheterized. Diuresis was stimulated by intravenous injection of normal saline solution. Urine collected from the ureter and washed bladder showed *albumin*

constantly present in about equal amounts. The dog had aspirated some vomitus into the bronchi during the ether anæsthesia and died the next day with extensive pneumonia of one side. The autopsy was made at once and showed normal kidneys, both the one removed at operation and that removed at autopsy. The ureters and pelves were normal. The bladder showed a moderate grade of subacute cystitis, especially about the opening of the urethra.

2-3-'12. Gave 500 cc. of water by stomach tube. Washed bladder 6 times, with 50 cc. of water each time, until the last washing showed negative albumin test. 3 cc. of urine collected during 5 minutes after last washing.

2-6-'12. Gave 500 cc. of water by stomach tube. Washed bladder as before.

2-8-'12. Weight 9.4 kilos (20¾ lbs.). Animal in good condition.

2-10-'12. Gave 500 cc. of water by stomach tube. Washed bladder as before. Urine collected for 15 minutes following washing.

DOG B-24.

Date. 1912.	Amt. of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.			Remarks.
	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.	
Jan. 9..	....	114	Acid.	Neg.	Neg.	....	.....	Neg.	Neg.	Neg.	Neg.	.....
Operation: Foreign body introduced into bladder.												
Jan. 12..	60	..	Ac.	Heavy.	Heavy.	....	.....	0	+	+	Few.	.....
Jan. 13..	95	..	Ac.	Heavy.	Heavy.	....	.....	0	+	+	Few.	.....
Jan. 13..	...	71	Ac.	Moderate.	Moderate.	....	.....	0	+	+	Few.	.....
Jan. 14..	130	..	Ac.	Moderate.	Moderate.	....	.....	0	+	+	Few.	.....
Jan. 14..	...	50	Ac.	Moderate.	Moderate.	....	.....	0	+	+	Few.	.....
Jan. 15..	60	..	Ac.	Moderate.	Moderate.	....	.....	0	Few.	Few.	Few.	.....
Jan. 16..	65	..	Ac.	Light.	Light.	....	.....	0	Few.	Few.	Few.	.....
Jan. 16..	80	..	Ac.	Light.	Light.	....	.....	0	Few.	Few.	Few.	.....
Jan. 18..	...	35	Ac.	Light.	Light.	....	.....	0	Few.	Few.	Few.	.....
Jan. 21..	250	..	Ac.	Light.	Moderate.	....	.....	0	Very few.	Very few.	Few.	.....
Jan. 21..	28	..	Ac.	Moderate.	Moderate.	....	.....	0	Very few.	+	Few.	.....
Jan. 22..	50	..	Ac.	Moderate.	Moderate.	⅓	.....	0	Few.	+	Few.	.....
Jan. 23..	35	..	Ac.	—	Moderate.	....	.....	0	—	—	—	.....
Jan. 24..	105	..	Ac.	Moderate.	Heavy.	1¾	Dirty gray.	0	+ +	+	+	.....
Jan. 25..	...	18	Ac.	—	Heavy.	....	.....	—	—	—	—	.....
Jan. 25..	...	15	Ac.	Moderate.	—	½	.....	.....	+ +	+	Few.	.....
Jan. 26..	250	..	Ac.	Faint.	Distinct.	⅓	.....	A few hyal. and gran.	+	+	Very few	.....
Jan. 27..	50	..	Ac.	Heavy.	Heavy cloud.	2	Dirty green.	—	—	—	—	.....
Jan. 27..	...	15	Neut.	—	—	....	.....	A few gran.	+	Few.	Few.	.....
Jan. 28..	250	..	Ac.	Faint.	Moderate.	½	Light gray.	A few hyal. and gran.	+	Few.	Few.	.....
Jan. 29..	85	..	Ac.	Moderate.	Moderate.	1½	.....	Very few hyal.	+ +	+	Few.	.....
Jan. 30..	...	32	Ac.	Moderate.	Moderate.	½	Green.	Very few gran.	+	Very few.	Few.	.....
Jan. 31..	410	..	Ac.	Moderate.	Moderate.	⅓	.....	Hyal. and gran.	Very few.	Few.	Few.	.....
Feb. 1..	...	15	Ac.	Moderate.	—	....	.....	Very few hyal.	+	Very few.	+	.....
Feb. 2..	280	..	Ac.	Moderate.	Moderate.	¾	.....	Neg.	Neg.	Neg.	Few.	.....
Feb. 3..	...	28	Ac.	Heavy.	Moderate.	1/10	White.	A few gran.	Neg.	+	+	.....
(a)..	...	6	Ac.	—	Moderate.	....	.....	—	—	—	—	Bladder washed and urine collected during diuresis.
(b)..	...	6	Ac.	—	—	....	.....	A few gran.	Neg.	+	+	
Feb. 4..	500	..	Neut.	Heavy.	Heavy.	1	.....	A few gran.	Neg.	Neg.	Few.	.....
Feb. 5..	50	..	Ac.	Heavy.	Heavy.	3	.....	Gran. and hyal.	Few.	Few.	+	.....
Feb. 6..	185	..	Ac.	Heavy.	Heavy.	1	Dark gray.	Very few hyal.	Neg.	Neg.	+ +	.....
Feb. 6..	...	25	Ac.	—	Heavy.	¾	Pale gray.	Many hyal. and gran.	Neg.	Neg.	+ +	Bladder washed and urine collected.
Feb. 7..	550	..	Ac.	Heavy.	Heavy.	⅓	.....	Very few hyal. and gran.	+	+	+	.....
Feb. 8..	...	30	Ac.	Heavy.	Heavy.	2	.....	Some gran.	+	+	+	.....
Feb. 9..	100	..	Ac.	Moderate.	Heavy.	1½	.....	A few gran.	+ +	+ +	+	.....
Feb. 10..	±	..	Ac.	Moderate.	Heavy.	½	.....	Neg.	+ +	+ +	+	.....
Feb. 10..	...	±?	....	—	Definite.	....	.....	—	—	—	—	Bladder washed and urine collected.
Feb. 12..	200	..	Ac.	Light.	Light.	¾	.....	A few gran.	Neg.	Few.	Neg.	.....
Feb. 13..	50	3	Ac.	—	Light.	....	.....	.....	+	+	Few.	.....
Feb. 13 Operation: Ureter catheterized.												
4.30 p. m.	....	8.0	.....	.....	.....	....	.....	.....	.....	.....	.....	Urine from ureter.
4.40 p. m.	....	2.5	.....	.....	Heavy.	....	.....	—	—	—	—	
5.00 p. m.	....	6.0	.....	.....	.....	4	White.	—	—	—	—	
5.20 p. m.	....	9.0	.....	.....	.....	2	White.	A few hyal. and many gran.	Neg.	+	+	
5.35 p. m.	....	2.8	.....	.....	Moderate.	....	.....	.....	—	—	—	
(a)..	....	40	.....	.....	Heavy.	1+	White.	.....	.....	.....	.....	Urine from bladder.
(b)..	....	17	.....	.....	Moderate.	1+	White.	A few hyal. and gran.	+ +	+	+ +	Urine from bladder after operation.

Dog C-16.

1-16-'12. Dog, female, fox terrier, mongrel, weight 8.4 kilos (18½ lbs.), in good condition. Urine negative.

1-20-'12. Operation: A marble was introduced into the bladder. Weight of animal 9.1 kilos (20 lbs.), in good condition.

1-21-'12. Animal in good condition. Wound dry.

1-22-'12. Animal lively.

1-25-'12. Weight 8.9 kilos (19.5 lbs.). Animal in good condition.

1-30-'12. Gave 350 cc. of water by stomach tube. Diuretic time 50 minutes. Motile bacteria in specimen of urine.

2-1-'12. Gave 350 cc. of water by stomach tube. Diuretic time 1 hour. Weight 9.1 kilos (20 lbs.).

2-15-'12. Weight 8.6 kilos (19 lbs.). Animal in good condition.

2-21-'12. Animal not very lively.

2-22-'12. Weight 8.9 kilos (19.5 lbs.). Animal in good condition.

3-30-'12. Weight 9.1 kilos (20¼ lbs.). Animal very fat and in good condition.

Operation: Catheterized left ureter.

11.48 a. m. Began salt infusion into right femoral vein.

12.05 p. m. 500 cc. salt infused.

12.09 p. m. Urine started to flow.

12.31 p. m. 1000 cc. salt infused (see table).

1.02 p. m. 1500 cc. salt infused.

1.12 p. m. 1600 cc. salt solution infused (total).

1.15 p. m. (see (a), table). Catheterized bladder urine.

1.35 p. m. Kidney removed, weight 34.5 gm. Normal throughout.

4-1-'12. Animal died during night.

Autopsy, 1.30 p. m. Right kidney weighed 32 gm. Cortex measured 7 mm. Normal. Ureters normal except for some dilatation of the lower 3 cm. of their length. Bladder: Subacute cystitis. Lungs: Beginning bronchopneumonia and œdema. Abdomen: Acute peritonitis, surgical sponge left in abdominal cavity. Other organs negative.

Microscopical sections: Kidney removed at operation shows perfectly normal stroma, tubules and glomeruli. Kidney removed at autopsy shows perfectly normal stroma and glomeruli. The epithelium of the convoluted tubules shows post-mortem change. There is a small fibroma in the pyramid. The bladder shows an intact epithelial covering which is somewhat thickened. The submucosa is greatly thickened and is full of dilated vessels. Wandering cells are very numerous here, chiefly mononuclears. The other organs are negative.

Summary, Dog C-16.—This experiment was practically identical with preceding one (Dog B-24). The urine was negative before operation and insertion of a marble into the bladder. Albumin was constantly present after this time. Casts appeared after a period of ten days. Urine obtained at different intervals (weeks or months after operation) from the washed bladder or from the catheterized ureter during diuresis, showed constantly albumin in considerable amounts ($\frac{1}{2}$ to 2 gm. to the litre). It seems certain, then, that the greater part of the albumin found in the daily urine was excreted by the activity of the renal epithelium and not by the bladder mucosa.

DOG C-16.

Date.	Amt. of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.			Remarks.
1912	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.	
Jan. 18..	....	45	Ac.	Neg.	Neg.	—	.....	Neg.	Neg.	Neg.	Neg.	.....
Jan. 20..	....	50	Ac.	Neg.	Neg.	$\frac{1}{3}$	Dirty green.	Neg.	Neg.	Neg.	Neg.	.....
Jan. 20 Operation: Marble placed in bladder.												
Jan. 22..	100	....	Ac.	Heavy.	Heavy.	....	.....	Neg.	+ +	Neg.	Neg.	.....
Jan. 23..	100	....	Ac.	—	Heavy.	....	.....	Neg.	+ +	Neg.	Neg.	.....
Jan. 24..	125	....	Ac.	Very heavy.	Very heavy.	$5\frac{3}{4}$	Pink.	Neg.	+ +	Few.	Veryfew	.....
Jan. 25..	96	....	Ac.	Very heavy.	Very heavy.	$6\frac{1}{2}$	.....	Neg.	+ +	Few.	Veryfew	.....
Jan. 26..	220	....	Ac.	Heavy.	Heavy.	3	.....	Neg.	+ +	Very few.	Veryfew	.....
Jan. 27..	110	....	Ac.	Heavy.	Heavy.	$4\frac{1}{2}$	.....	Neg.	+	Few.	Few.	.....
Jan. 28..	250	....	Ac.	Heavy.	Heavy.	3	Pink.	Neg.	+	+	Few.	.....
Jan. 29..	180	....	Ac.	Moderate.	Heavy.	3	.....	Neg.	+	+	+	.....
Jan. 30..	250	....	Ac.	Moderate.	Heavy.	$\frac{1}{3}$	Light gray.	Neg.	Few.	Neg.	Few.	.....
Jan. 30..	150	....	Ac.	Light.	Light.	....	.....	Few gran.	Neg.	Neg.	Few.	.....
Jan. 31..	345	....	Ac.	Moderate.	Moderate.	$\frac{1}{2}$	.....	Few hyal.	+	Very few.	Neg.	.....
Feb. 1..	180	....	Ac.	Moderate.	Moderate.	$\frac{3}{4}$	.....	—	—	—	—	.....
Feb. 2..	200	....	Ac.	Moderate.	Moderate.	$\frac{3}{4}$	.....	A very few hyal.	Few.	Few.	Few.	.....
Feb. 3..	120	....	Ac.	Moderate.	Heavy.	$\frac{1}{2}$	White.	Numerous hyal. and gran.	Neg.	Neg.	+	.....
Feb. 3..	....	3	Ac.	—	Heavy.	....	.....	—	—	—	—	Bladder washed and urine collected during diuresis.
Feb. 4..	360	....	Ac.	Moderate.	Moderate.	$\frac{1}{2}$	.....	Hyal. and gran.	+	+	+ +	.....
Feb. 5..	150	....	Ac.	Heavy.	Heavy.	$3\frac{1}{2}$	.....	Gran.	+ +	+	+	.....
Feb. 6..	135	....	Ac.	Moderate.	Moderate.	$\frac{3}{4}$	Dirty gray.	Hyal. and gran.	+	+	Few.	.....
Feb. 6..	....	15	Ac.	—	Definite.	$\frac{3}{4}$	Light gray.	A few gran.	Neg.	Neg.	+ +	Bladder washed and urine collected during diuresis.
Feb. 7..	600	....	Ac.	Light.	Definite.	$\frac{1}{2}$	.....	Gran. and hyal.	Neg.	Few.	+	.....
Feb. 8..	250	....	Neut.	Moderate.	Definite.	1	.....	A few gran.	Neg.	Few.	+	.....
Feb. 9..	150	....	Ac.	Definite.	Definite.	1	.....	A few gran.	+	+	+	.....
Feb. 10..	....	8	.....	—	Definite.	....	.....	Hyal. and gran.	+	+	+	Bladder washed and urine collected during diuresis.
Feb. 12..	400	....	Ac.	Heavy.	Heavy.	1	Light green.	Hyal. and gran.	Neg.	Few.	+ +	.....
Feb. 13..	100	....	Ac.	—	Heavy.	....	.....	Few.	Neg.	Few.	Few.	.....
Feb. 14..	70	....	Ac.	Heavy.	Heavy.	2	Dark green on top.	Hyal. and gran.	—	+	+ +	.....
Feb. 15..	100	....	Ac.	Heavy.	Heavy.	$\frac{1}{3}$	.....	Few gran.	Neg.	+	+	.....
Feb. 16..	150	....	Ft. Ac.	Heavy.	Moderate.	$\frac{1}{2}$	.....	Numerous hyal. and gran.	Neg.	Very few.	Veryfew	.....
Feb. 17..	30	....	Ac.	Moderate.	Moderate.	....	.....	Few gran.	Neg.	Very few.	Few.	.....
Feb. 19..	50	....	Ac.	Moderate.	Heavy.	$\frac{1}{3}$	.....	+	Neg.	+	Neg.	.....
Feb. 20..	200	....	Alk.	Light.	Light.	$\frac{1}{3}$	White.	+	Few.	+	+	.....
Feb. 21..	37	....	Ac.	Very light.	Light.	$\frac{1}{10}$	White.	+	Neg.	+	+	.....
Feb. 22..	150	....	Ac.	Light.	Moderate.	$\frac{1}{2}$	White.	+	Neg.	+	Few.	.....
Feb. 23..	150	....	Ac.	Light.	Light.	$\frac{1}{2}$	Gray.	—	—	—	—	.....
Feb. 24..	....	22	Ac.	Faint.	Very light.	$\frac{1}{10}$	White.	+	Neg.	+	Few.	.....
Feb. 26..	250	....	Ft. Ac.	Light.	Moderate.	1	.....	Hyal. and gran.	Neg.	Very few.	Neg.	.....
Feb. 27..	135	....	Neut.	Moderate.	Moderate.	1	White.	Hyal. and gran.	Neg.	+	Few.	.....
Feb. 29..	200	....	Neut.	Light.	Light.	$\frac{1}{2}$	.....	Hyal. and gran.	Neg.	+	+	.....
Mar. 1..	100	....	Ac.	Light.	Light.	$\frac{1}{2}$	.....	Hyal. and gran.	Neg.	+	+	.....
Mar. 7..	....	45	Ac.	Light.	Moderate.	1	Light gray.	Few.	Few.	+	+	.....
Mar. 16..	....	22	Ac.	Very light.	Light.	$\frac{1}{10}$	.....	One gran.	Neg.	Few.	Few.	.....
Mar. 18..	....	12	Alk.	—	Very faint.	$\frac{1}{4}$	.....	Hyal. and gran.	Few.	+	Few.	.....
Mar. 21..	....	7	Ac.	Very faint.	—	....	.....	Few.	Few.	+ +	Few.	.....
Mar. 26..	....	9	Ac.	—	Light.	....	.....	Few.	Neg.	+	+	.....
Mar. 29..	....	10	Alk.	Very heavy.	Very heavy.	....	.....	Hyal. and gran.	Neg.	+	+	.....
Mar. 30 Operation: Ureter catheterized.												
12.30 p.m.	....	8	Ac.	Light.	Faint.	—	.....	.....	Few.	Neg.	Neg.	Urine from ureter.
1.12 p.m.	....	12	Ac.	Light.	Faint.	$\frac{1}{2}$	.....	Neg.	Few.	Neg.	Neg.	Urine from ureter.
(a).	....	60	Ac.	Light.	Faint.	1	.....	Very few gran.	Neg.	+ +	Few.	Urine from bladder.

Dog C-41.

3-5-'12. Dog, female, bull terrier, weighs 7.8 kilos (17¼ lbs.), in splendid condition.

Operation: Marble introduced into bladder.

3-16-'12. Wound healed, dog in good condition.

3-21-'12. Weighed 8.1 kilos (17¾ lbs.). Gave 500 cc. of water by stomach tube. Diuretic time 55 minutes. Animal in good condition.

3-26-'12. Gave 700 cc. of water by stomach tube and washed bladder as described. Urine collected during the 20 minutes following washing. Animal in good condition.

3-28-'12. Weighs 8.1 kilos (17¾ lbs.). Gave 500 cc. of water by stomach tube and washed bladder with negative result. Animal in good condition.

7-17-'12. Dog in good condition, weight 18 lbs. Abdominal operation. Normal saline intravenously to promote diuresis. Urine collected every ½ hr. shows albumin constantly present.

5 p. m. Death and *autopsy* at once. Right kidney is definitely hypertrophied, but surface is smooth after removal of capsule. Cortex on section is thickened. Pelvis and ureter normal. Bladder is thickened somewhat and contracted about the marble, which is frosted with deposits of gray color. There are no ulcers.

DOG C-41.

Date.	Amt. of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.			Remarks.
1912	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.	
Mar. 5..	....	70	Ac.	Neg.	Very faint.	¼	.....	Neg.	Neg.	Neg.	Neg.	.....
Mar. 5 Operation: Marble placed in bladder.												
Mar. 9..	250	....	Ac.	Heavy.	Moderate.	2½	.....	Hyal. and gran.	Few.	Few.	Few.	.....
Mar. 16..	....	38	Ac.	—	Slight.	½	.....	Neg.	Neg.	Neg.	.....	.....
Mar. 18..	....	48	Alk.	Very faint.	Faint.	Tr.	.....	Few hyal.	Few.	Neg.	Neg.	.....
Mar. 19..	....	30	Ac.	Very light.	Moderate.	½	Dirty olive green	Few hyal.	Few.	Few.	+	.....
Mar. 21..	....	52	Ac.	Very light.	Moderate.	⅓	.....	Neg.	Neg.	Neg.	Few.	.....
Mar. 22..	530	....	Neut.	Light.	Moderate.	Neg.	.....	—	—	—	—	.....
Mar. 23..	....	15	Ac.	Light.	—	⅓	Greenish tinge.	Numerous.	+	+	+	.....
Mar. 25..	....	58	Ft. ac.	Very faint.	Moderate.	⅔	.....	+	Neg.	+	+	.....
Mar. 26..	....	40	Ac.	Light.	Moderate.	1	Light gray.	+	Neg.	+	+	.....
Mar. 26..	....	±	.....	.....	Moderate.	....	.....	.....	.....	.....	.....	Bladder washed and urine collected.
Mar. 28..	....	7	Ac.	—	Faint.	....	.....	+	Few.	Few.	+	.....
Mar. 29..	....	136	Ft. alk.	Faint.	Light.	1/10	Light gray.	Very few.	Neg.	Very few.	Few.	.....
Apr. 2..	....	13	Ac.	—	Light.	1¾	Gray.	Very few.	Neg.	Very few.	Few.	.....
Apr. 11..	....	24	Ac.	Heavy.	Moderate.	½	Dirty yellow.	Few.	Few.	+ +	Few.	.....
Apr. 15..	....	117	Alk.	Neg.	Neg.	¼	Dirty green.	Neg.	Neg.	Neg.	Neg.	.....
Apr. 20..	....	17	Ac.	—	Light.	Tr.	Light green.	Neg.	Neg.	Few.	Neg.	.....
Apr. 23..	....	95	Ac.	Neg.	Very light.	1/10	Greenish gray.	Neg.	Neg.	Neg.	Neg.	.....
Apr. 29..	....	53	Neut.	Very faint.	Light.	1/10	Light yellow.	Few.	Very few.	Neg.	Very few.	.....
May 4..	....	50	.....	.....	.....	....	.....	.....	.....	.....	.....	.....
May 4..	....	8	Ac.	—	Light.	....	.....	Neg.	Neg.	Neg.	Few.	Bladder washed and urine collected.
May 6..	....	35	Alk.	Heavy.	Heavy.	1½	Grayish green.	Neg.	Few.	+	Few.	.....
May 7..	....	65	Ac.	Light.	Moderate.	¾	White.	Neg.	Very few.	Neg.	Neg.	.....
May 7 Operation: Removal of left kidney.												
May 11..	....	55	Alk.	Moderate.	Moderate.	¼	Light gray.	Neg.	Neg.	Few.	Few.	.....
May 14..	....	93	Ac.	Light.	Light.	1/10	Gray.	Very few.	Neg.	Very few.	Few.	.....
May 16..	....	85	Alk.	Light.	Light.	⅔	Gray.	Two casts.	Neg.	Neg.	Few.	.....
May 16..	....	25	Ac.	Light.	Light.	¼	White.	+	Neg.	Neg.	+ +	Bladder washed and urine collected during diuresis.
May 18..	....	15	Ac.	Light.	Moderate.	½	Greenish tinged.	Neg.	Neg.	+	+	.....
May 24..	....	50	Ac.	Moderate.	Moderate.	⅓	Dark gray.	Neg.	Neg.	Neg.	Few.	.....
May 27..	....	29	.....	.....	.....	....	.....	.....	+ + +	.....	.....	.....
May 29..	....	39	Ac.	Heavy.	Heavy.	2	Gray.	Few hyal.	+	Neg.	Neg.	.....
July 17.. 8.15 a.m.	....	12	.....	.....	.....	2	.....	.....	Neg.	.....	.....	.....
10.45 a.m. Operation: Eck fistula produced—saline intravenously.												
11.53 a.m.	....	30	.....	.....	.....	2½	.....	.....	.....	.....	.....	.....
12.45 p.m.	....	5	.....	.....	.....	2½	.....	.....	.....	.....	.....	.....
1.45 p.m.	....	12	.....	.....	.....	2½	.....	.....	.....	.....	.....	.....
2.45 p.m.	....	20	.....	.....	.....	2½	.....	.....	.....	.....	.....	.....
3.45 p.m.	....	57	.....	.....	.....	2½	.....	.....	.....	.....	.....	.....

4-11-'12. Animal weighs 8.2 kilos (18 lbs.) and is in good condition.

4-30-'12. Weighs 8.7 kilos (19¼ lbs.), has mange.

5-4-'12. Gave 600 cc. of water by stomach tube and washed bladder as described. 8 cc. of urine collected during the following 12 minutes. Condition excellent.

5-7-'12. Operation: Removal left kidney. Weight 23 gm. Normal in gross and microscopically.

5-11-'12. Weighs 8.4 kilos (18¼ lbs.). Condition good.

5-16-'12. Weighs 8.6 kilos (18¾ lbs.). Condition excellent. Gave 700 cc. of water by stomach tube and bladder washed. 9 cc. of urine collected during the following 12 minutes.

The mucosa of fundus is normal, of base is mottled with reddish areas and indefinite nodules—a subacute cystitis.

Microscopical sections: The glomeruli, tubules and stroma are quite normal. Some of the tubules are a little dilated and contain pale, hyaline material (casts). There is no evidence of any beginning chronic nephritis. Bladder shows areas in which the epithelium is thickened. The submucosa is infiltrated with a good many mononuclear cells, some of which contain blood pigment. The blood-vessels are rather conspicuous with thickened walls. The muscle of the bladder shows definite hypertrophy.

Summary, Dog C-41.—This animal presented a very slight albuminuria before operation, but in general the observations

confirm those of the previous ones. This animal was not as sensitive to bladder irritation as many dogs, but is of interest because of the prolonged observation and a general tendency of the albuminuria to increase.

Removal of one kidney had no appreciable effect on the other organ, unless a slight amount of the albumin could be attributed to the extra work thrown upon the single organ. Autopsy showed the usual subacute cystitis, but normal ureter and pelvis with a kidney practically normal except for a uniform hypertrophy. The tubules contained a few casts, but there was no increase in connective tissue.

Dog C-54.

4-3-'12. Dog, female, mongrel, weight 7.7 kilos (17 lbs.), in good condition.

4-4-'12. Operation: Collar button sutured into bladder wall.

4-11-'12. Weighs 7.3 kilos (16 lbs.). Wound in good condition. Animal lively.

4-19-'12. Gave 500 cc. of water by stomach tube. Diuretic time 30 minutes. Weighs 7.9 kilos (17½ lbs.).

4-30-'12. Gave 500 cc. of water by stomach tube. Animal weighs 7.2 kilos (16¼ lbs.).

5-3-'12. Animal has diarrhœa and distemper.

5-11-'12. Gave 700 cc. of water by stomach tube. Animal has distemper.

5-14-'12. Gave 700 cc. of water by stomach tube and washed out bladder, but could not collect enough urine for test after washing.

5-21-'12. Gave 600 cc. of water by stomach tube, washed bladder and collected 8 cc. of urine during the 15 minutes following the washing.

5-23-'12. Operation: Catheterized left ureter about 4 cm. from pelvis of kidney.

4.50 p. m. Began infusion of salt solution into right femoral vein.

5.00 p. m. 500 cc. of salt solution infused.

5.20 p. m. 1000 cc. of salt solution infused.

5.30 p. m. Urine began to flow.

5.35 p. m. 1500 cc. of salt solution infused.

5.36 p. m. Catheter passed and 5 cc. of urine taken.

6.00 p. m. 2000 cc. of salt solution infused.

6.25 p. m. 3000 cc. of salt solution infused.

6.30 p. m. Urinated about 30 cc.

6.55 p. m. 3250 cc. of salt solution infused (total).

7.00 p. m. 7 cc. of urine collected and cannula taken from ureter. Kidney removed. Weighed 28 gm. Normal.

5-24-'12. Animal found dead in cage at 9.00 a. m.

12 Noon, *autopsy*. Right kidney weighed 30 gm. Normal in gross. Ureters normal. Bladder contracted, did not contain any urine. Button was firmly encapsulated in fibrous tissue on the serous surface, by the œdematous bladder wall. There was some injection of the mucosa around neck and area surrounding button. A very small calculus was found in the bladder near the button. It was about 4 mm. in length and 1 mm. in largest diameter. It was formed around a small piece of silk suture in the wall of the bladder. Chronic cystitis around area near button. Other organs normal.

DOG C-54.

Date. 1912.	Amt. of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.			Remarks.
	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.	
Apr. 3..	..	64	Ac.	Neg.	Neg.	¾	Brown.	Neg.	Neg.	Neg.	Neg.	Very concentrated urine.
Apr. 4..	..	28	Ac.	Neg.	Neg.	1/20	Brown.	Neg.	Neg.	Neg.	Many.	.....
Apr. 4. Operation: Button fixed in bladder wall.												
Apr. 12..	..	4½	Ac.	.....	.....	....	.....	Neg.	Few.	+	+	.....
Apr. 14..	..	4	Alk.	.....	.....	....	.....	Few hyal. and gran.	+	+	+	.....
Apr. 15..	..	17	Alk.	Light.	Light.	¼	Dirty blue.	Few.	Very few.	Very few.	Few.	.....
Apr. 16..	..	3	Alk.	.....	.....	....	.....	.....	Few.	Few.	+ +	.....
Apr. 18..	65	....	Ac.	Light.	Light.	Trace.	White.	Few.	Neg.	Neg.	Few.	.....
Apr. 29..	..	2	Ac.	.....	.....	....	.....	Few.	+	+	+	.....
Apr. 30..	..	16	Ac.	Moderate.	Moderate.	1/10	Light brown	Neg.	+ +	Few.	Few.	.....
May 4..	..	4	Ac.	.....	.....	....	.....	Numerous gran.	+	Few.	Few.	.....
May 6..	..	4	Ac.	.....	.....	....	.....	Few.	+	+	Few.	.....
May 11..	..	9	Ac.	Light.	Moderate.	....	.....	Few hyal.	Neg.	Neg.	+ +	.....
May 11..	58	....	Alk.	Light.	Heavy.	⅕	White.	—	—	—	—	.....
May 16..	..	6¼	Ac.	Light.	Light.	....	.....	.....	.....	.....	.....	.....
May 21..	..	8	Ac.	Moderate.	Light.	1½	White.	One hyal.	Few.	Few.	+	Bladder washed and urine collected.
May 23..	..	50	Ac.	Moderate.	Moderate.	¾	White.	Few.	Very many.	Few.	Neg.	.....
May 23. Operation: Catheter in ureter.												
May 23..	..	7	Ac.	Moderate.	—	1½	White.	Few,	Very few.	Neg.	Neg.	Urine from ureter.

Microscopical sections: Kidney shows no abnormality of the stroma or glomeruli. Some of the tubules contain a good deal of granular coagulum, and others indefinite casts associated with a certain amount of dilatation of the lumen. Bladder shows a moderate grade of thickening of the submucosa with infiltration by mononuclear cells. The epithelial covering appears normal.

Summary, Dog C-54.—This dog differed somewhat in that the foreign body was fixed in the fundus of the bladder—a metal collar button with its broad base inside the bladder cavity, and its head in the peritoneal cavity. This operation caused a certain amount of cystitis and localized peritonitis, with a resultant albuminuria. It will be noted that the albuminuria was more pronounced following a bladder irrigation, and in general showed a tendency to increase slowly in amount. Urine obtained from the ureter at operation showed a considerable amount of albumin. Autopsy showed localized cystitis about the button and a small calculus adherent to a thread in the bladder wall. The kidneys were normal except for a few hyaline casts and slight dilatation of the tubules in places.

Dog C-59.

4-16-'12. Young female fox terrier, weight 6.8 kilos (15 lbs.), in poor condition. Unable to catheterize.

4-18-'12. Dilated vagina under ether.

4-25-'12. Dog in fair condition. Operation: Marble introduced into the bladder and a "bachelor's button" sutured into the wall of the bladder.

4-28-'12. Observed animal pass a few drops of bloody urine, and upon catheterizing the marble was dislodged from the neck of the bladder and about 20 cc. of urine drawn off.

5-13-'12. Found in cage very sick. About 25 cc. bloody fluid drawn off when catheter was introduced. Made subcutaneous injection of sterile salt solution and irrigated bladder. Died 5.00 p. m.

Autopsy, 5.10 p. m. Kidneys: Right weighs 28 gm. Left 25 gm. They are quite normal in gross. Ureters are normal. Bladder is dilated with bloody fluid, and in places the wall seems friable and partly necrotic. The mucosa is deep red mottled and greenish in places. The serous surface is injected. The urethra is practically normal. The peritoneal cavity contains 225 cc. of blood-stained fluid, and the serous surface shows beginning fibrinous inflammation. A part of this fluid certainly was derived from the urinary bladder, although no definite leak could be demonstrated at the time of autopsy.

Microscopical notes: Kidney: There is no increase in connective tissue. Glomeruli are normal. Many of the convoluted tubules contain definite casts and are dilated. One sees, too, considerable granular pink-staining material in the lumina of the convoluted tubules. The blood-vessels are widely distended. The collecting tubules and pyramids show numerous characteristic hyaline casts. The bladder shows extensive ulcers with necrosis involving the mucosa and submucosa. The submucosa is œdematous and infiltrated with great numbers of wandering cells, many of which are polymorphonuclears and show some increase in connective tissue as well. Some sections show extensive hemorrhage and œdema involving a part of the muscle coat as well.

Summary, C-59.—In this experiment a marble was placed in the bladder, and in addition a large button was fixed in the fundus of the bladder. This was associated with a high grade of albuminuria, of which a part was probably derived from the inflamed bladder mucosa. No washing of the bladder nor ureteral catheterization were accomplished, as the animal died from acute cystitis with leakage of urine into the abdomen and general peritonitis. It is of interest to note that the inflammation had not extended up the ureters in spite of obvious obstruction, and that the kidneys were free from acute inflammation. This is to be compared with the following case where an ascending infection was present. The kidneys under the microscope showed numerous hyaline casts and evidence of considerable albuminuria, but no evidence of acute or chronic nephritis. So it is very evident that much of the excreted albumin was derived from the kidney.

DOG C-59.

Date. 1912.	Amount of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.		
	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.
Apr. 20..	....	47	Ac.	Neg.	Neg.	Trace.	Dirty gray.	Neg.	Neg.	Neg.	Neg.
Apr. 23..	....	3	Ac.	.....	.....	.....	.....	Neg.	Neg.	Neg.	Few.
Apr. 25. Operation: Foreign bodies placed in bladder wall and lumen.											
Apr. 29..	....	17	Alk.	Heavy.	Moderate.	2½	Gray.	Neg.	+ +	Few.	+
Apr. 30..	....	55	Ac.	Heavy.	Moderate.	1½	Light gray.	—	+ + +	—	—
May 7..	....	46	Alk.	Moderate.	Heavy.	1	White.	Neg.	+	+	Few.
May 11..	....	7	—	—	Moderate.	...	.....	Neg.	Neg.	+	Few.

DOG C-34

Date. 1912	Amt. of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.			Remarks.
	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.	
Feb. 15..	....	35	Ac.	Neg.	Very faint.	1/10	Dirty green.	Neg.	Neg.	Neg.	Neg.	.....
Feb. 17..	....	30	Ac.	Faint.	Light.	1/3	Gray.	Neg.	Neg.	Neg.	+	.....
Feb. 19..	170	....	Ac.	Light.	Heavy.	3/4	Gray.	Many.	Few.	+	+	Cystitis from catheter.
Feb. 20..	....	12	Ac.	—	Light.	1/6	.....	+	+ +	+	+	.....
Feb. 20 Operation: Marble placed in bladder.												
Feb. 22..	125	....	Ac.	Very heavy.	Heavy.	8	Drab.	.....	+ + +	.....	.....	.....
Feb. 23..	200	....	Ac.	Very heavy.	Heavy.	4	Dirty green.	.....	.....	.....	.....	.....
Feb. 24..	240	....	Alk.	—	Very heavy.	3	.....	.....	.....	.....	.....	.....
Feb. 24..	45	....	Neut.	Heavy.	Heavy.	3	.....	.....	+	+	Few.	.....
Feb. 25..	....	8	Ac.	Moderate.	Moderate.	—	.....	.....	.....	.....	.....	.....
Feb. 25..	....	55	Ft. Ac.	Moderate.	Moderate.	1½	.....	Neg.	Neg.	+ +	Neg.	.....

Dog C-34.

2-15-'12. Dog, female, mongrel, weight 5.9 kilos (13 lbs.), in good condition.

2-17-'12. 400 cc. water by stomach tube. Diuretic time 1 hour.

2-20-'12. Operation: Marble introduced into the bladder. Animal in good condition.

2-22-'12. Animal weighs 5.4 kilos (12 lbs.). Wound in good condition.

2-24-'12. Animal very sick, vomiting and diarrhœa. Wound in good condition.

2-25-'12. Animal very sick.

Operation: Made unsuccessful attempt to catheterize ureter and collect urine. About 2 cc. of blood-tinged urine was collected. Animal died 3.10 p. m.

Autopsy, 3.25. Kidneys: Pyelonephritis. Ureters: Purulent ureteritis. Bladder: Acute ulcerative cystitis. Acute local peritonitis in region of bladder and slight general peritonitis. Lungs: Œdema. Other organs normal.

Microscopical sections: Kidneys show the usual picture of suppurative pyelonephritis, with great numbers of polymorphonuclear leucocytes in large masses and columns extending throughout the cortex and medulla. In places the tubules show a good deal of injury, and again they are relatively normal. There is considerable œdema and congestion. The ureter shows a definite acute inflammation, particularly of the submucosa, and pus cells in considerable numbers are found in the lumen, in the mucosa and the œdematous submucosa. Bladder wall shows loss of substance, in places extensive hemorrhage into the submucosa associated with a great deal of œdema and numbers of wandering cells.

Summary, Dog C-34.—This dog shows a characteristic picture of acute cystitis with an ascending ureteritis, pyelitis and pyelonephritis with miliary abscesses. There was an acute localized peritonitis. It is probable that this dog was infected before operation by catheter and the foreign body intensified the inflammation, with its spread into the bladder wound and ureters. No urine was obtained from the washed bladder or ureter by catheter.

Dog C-38.

3-2-'12. Dog, male, mongrel, weight 7.7 kilos (17 lbs.), poorly nourished. Collected 8 cc. urine in beaker while animal was being anæsthetized.

Operation: Catheterized left ureter about 3 cm. from pelvis of kidney.

12.50 p. m. Started salt solution infusion, right femoral vein.

12.52 p. m. Urine started to flow.

1.04 p. m. 500 cc. salt solution infused.

1.38 p. m. 1000 cc. (total amount) salt solution injected.

Operation: Left kidney removed; it was normal. 550 cc. of urine collected from cage a few hours after operation.

3-7-'12. Animal in fair condition, weighs 7.3 kilos (16¼ lbs.). Wound broken down through skin and subcutaneous tissues.

3-21-'12. Animal weighs 7.7 kilos (17 lbs.). Wound healed. Condition fair.

3-23-'12. Operation: Catheterized right ureter about 3 cm. from pelvis of kidney.

10.55 a. m. Began infusion of salt solution into left femoral vein.

11.00 a. m. Urine started to flow.

11.05 a. m. 500 cc. of salt solution infused.

11.20 a. m. 1000 cc. of salt solution infused.

11.55 a. m. 1500 cc. of salt solution infused.

DOG C-38.

Date.	Amt. of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.			Remarks.
1912	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.	
Mar. 2..	165	....	Ac.	Very light.	Light.	1/10	Greenish.	Hyal. and gran.	Neg.	Few.	Neg.	Spermatozoa numerous. Balanitis +.
Mar. 2..	....	8	Ac.	—	Light.	1/5	.....	Few.	Neg.	Few.	Neg.	Caught in beaker.
Mar. 2 Operation: Ureter catheterized.												
12.56 p.m.	....	3½	Neut.	.....	.....	....	.....	Neg.	+	Neg.	Few.	.....
1.02 p.m.	....	5	Neut.	Light.	Trace.	....	.....	.....	.....	.....	.....	.....
1.11 p.m.	....	10	Neut.	.....	Trace.	1/15	.....	.....	.....	.....	.....	.....
1.18 p.m.	....	10	Neut.	Light.	Trace.	—	.....	Neg.	Neg.	Neg.	Neg.	.....
1.27 p.m.	....	10	Neut.	—	Trace.	1/15	.....	.....	.....	.....	.....	.....
1.43 p.m.	....	17	Ac.	Light.	Neg.	1/15	.....	Neg.	+	+ ?	Few.	.....
5.00 p.m.	550	....	Ac.	Neg.	Very light.	Tr.	.....	Neg.	Neg.	Neg.	Neg.	Post-operative cage urine.
Mar. 5..	18	....	Alk.	Very light.	Light.	¼	.....	+	Neg.	Neg.	Neg.	.....
Mar. 7..	140	....	Alk.	Light.	Moderate.	⅓	Pink.	Neg.	Neg.	Neg.	Neg.	.....
Mar. 8..	90	....	Ac.	Very light.	Very light.	½	.....	Few.	Neg.	Neg.	Neg.	.....
Mar. 9..	150	....	Ac.	Faint.	Very light.	⅔	.....	Few.	Neg.	Neg.	Neg.	Spermatozoa numerous.
Mar. 11..	60	....	Ac.	Light.	Moderate.	1	.....	.....	.....	.....	.....	.....
Mar. 23 Operation: Ureter catheterized.												
11.09 a.m.	....	4	Ac.	—	—	—	.....	.....	.....	.....	.....	.....
11.30 a.m.	....	11	Ac.	Light.	?	1/10	.....	.....	.....	.....	.....	.....
11.53 a.m.	....	11	Ac.	Light.	Light.	—	.....	.....	.....	.....	.....	.....
12.13 p.m.	....	14	Ac.	Light.	Light.	1/15	.....	A very few hyal.	+	Neg.	Neg.	.....
.....	....	50	Ac.	Heavy.	Heavy.	1½	.....	Few.	+	Neg.	Few.	Very conc. urine obtained from bladder at autopsy.

DOG S-11.

Date, 1912.	Amount of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.		
	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.
Apr. 13..	65	....	Ac.	Very light.	Light.	½	Light yellow.	Few.	Neg.	Few.	Neg.
Apr. 13. Operation: Ureter catheterized.											
12.11 p.m.	....	3	Ac.	—	Very light.	—	.....	.....	.....	.....	.....
11.35 p.m.	....	11	Ac.	—	Very light.	Trace.	White.	Neg.	Neg.	Neg.	Very few.
1.15 p.m.	....	9	Ac.	Very light.	Very light.	Trace.	White.	.....	.....	.....	.....

Animal bled to death from femoral artery. Removed bladder entire, with 50 cc. of concentrated urine.

2.00 p. m. *Autopsy.* Right kidney: Weight 40 gm. Two small infarcts were present. Otherwise the cortex was normal except for a little hypertrophy. Ureters normal. Bladder normal. Other organs normal.

Summary, Dog C-38.—This experiment and the one following serve as controls for the catheterization of the ureters. It is seen that this procedure does not call out any albuminuria. Extirpation of one kidney may cause a slight albuminuria, associated, perhaps, in part with the excess work thrown upon the other organ. Catheterization of the second ureter shows an interesting finding. The concentrated bladder urine contains much more albumin than does the urine obtained during diuresis from the ureter. The diuresis dilutes the albumin which is being excreted. It is interesting to compare this finding with those in other experiments where bladder irritation by a catheter is present and we find more albumin in the ureteral urine at this time than in that collected just previously from the bladder.

Dog S-11.

4-13-'12. Dog, male, mongrel, weight 6.4 kilos (14 lbs.), in poor condition.

Operation: Catheterized left ureter about 3 cm. from pelvis of kidney and later removed left kidney.

12.00 m. Began infusion of salt solution into right jugular vein.

12.07 p. m. Urine began to flow.

12.10 p. m. 500 cc. salt solution infused.

12.30 p. m. 1000 cc. salt solution infused.

12.50 p. m. 1400 cc. salt solution infused (total amount).

1.15 p. m. Urine collected (see table).

Operation: Left kidney removed, weight 37 gm. Normal in gross. Microscopically there is no increase in connective tissue. The glomeruli and convoluted and collecting tubules are normal.

4-18-'12. Animal weighs 6.4 kilos (14 lbs.).

4-27-'12. Animal in good condition. Wound healed excepting two or three stitch abscesses. Used for another experiment.

Dog C-50.

4-30-'12. Young dog, female, mongrel, weight 8.6 kilos (19 lbs.), in excellent condition.

DOG C-50.

Date. 1912	Amount of urine in cc.		Reaction of urine.	Albumin.				Casts.	Cells.		
	Cage.	Catheter.		Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.
May 4..	....	43	Ac.	Light.	Moderate.	Trace.	White.	Neg.	+ +	+	Few.
May 10..	....	20	Ac.	Light.	Light.	Trace.	White.	Neg.	Few.	+ +	Few.
May 11..	....	72	Ac.	Very faint.	Light.	—	.....	Neg.	Neg.	+	Few.
May 11. Operation: Bladder treated with 1 per cent silver nitrate for ten minutes.											
May 14..	....	15	—	Moderate.	Light.	—	.....	.....	.....	.....	.....
May 14. Operation: Bladder treated as before.											
May 16..	....	10	Ac.	Heavy.	Moderate.	—	.....	Two casts.	+	Few.	Few.
May 16..	30	....	Ac.	Heavy.	Heavy.	2½	Drab.	—	.....	.....	.....
May 17..	675	....	Ac.	Heavy.	Heavy.	¾	Drab.	Many.	Neg.	Few.	+

DOG C-80.

Date, 1912.	Amt. of urine in cc. Catheter.	Reaction of urine.	Albumin.				Casts.	Cells.			Remarks.
			Heller's test.	Heat and acetic acid test.	Gms. per litre.	Color of Esbach ppt.		Blood.	Pus.	Epithelium.	
May 24..	50	Ac.	Light.	Moderate.	$\frac{1}{10}$	Dark gray.	Neg.	+ +	Neg.	Few.	.....
May 24. Operation: Bladder treated with 1 per cent silver nitrate solution for five minutes.											
May 29..	30	Alk.	Moderate.	Moderate.	$\frac{1}{10}$	Gray.	Neg.	+	+	Neg.	.....
May 29..	24	Ac.	Heavy.	Moderate.	1	White.	Neg.	Neg.	Neg.	Few.	Bladder washed and urine collected during diuresis.
May 30..	40	Ac.	Very light	Light.	$\frac{1}{10}$	Gray.	Few.	Few.	+	Few.	.....
a.	5	Ac.	—	Light.	—	—	Neg.	Neg.	Neg.	Neg.	Bladder washed and urine collected during diuresis.
b.	11	Ac.	Light.	—	½	White.	Very few.	Few.	Neg.	+	(See Notes.)

5-11-'12. Weighs 8.7 kilos (19¼ lbs.). Irrigated bladder with 100 cc. of a 1 per cent silver nitrate solution in water for 10 minutes, under ether.

5-14-'12. Vagina very sensitive. Irrigated bladder with 50 cc. of a 1 per cent silver nitrate solution in water for 10 minutes, under ether. Animal not very active.

5-21-'12. Animal found very sick. Operation: Attempted to catheterize right ureter and collect urine, but animal died about 10 minutes after start.

Autopsy at once. Kidneys: The right kidney weighs 25 gm. and is normal in gross. The left kidney weighs 63 gm. and presents the characteristic picture of pyelonephritis. Its cortex is widened and streaked with opaque yellow lines containing purulent material, alternating with reddish zones of hemorrhage. The pyramids and pelvis are involved in this acute inflammation. Bladder: The mucosa is ulcerated and the bladder wall gangrenous, being of a mottled reddish green color. The serous surface of the bladder shows an acute fibrinous inflammation, but the

peritonitis is localized in the pelvis. The other organs are negative.

Microscopical section: Kidney shows an extreme grade of œdema, hemorrhage and infiltration of the greater part of the cortex with pus cells. Many of the tubules are destroyed. The purulent inflammation involves the tips of the pyramids and pelvis. Bladder shows extreme œdema of all its coats, with necroses involving the mucosa, submucosa and parts of the muscular coats, associated with more or less hemorrhage and great numbers of pus cells. The left ureter shows œdema of its submucous tissue with injection of the blood-vessels and numerous wandering cells, particularly polymorphonuclears.

Summary, Dog C-50.—Silver nitrate was used to produce a severe chemical cystitis, which developed into an ulcerative and gangrenous cystitis. It is curious to note that the ascending infection involved only one kidney, perhaps dependent in part on the animal's position in the cage. There is not an extreme grade of albuminuria, considering the lesions present in the bladder and one kidney.

Dog C-80.

5-24-'12. Young dog, female, collie, weighs 11.3 kilos (25 lbs.), in excellent condition.

Operation: Under ether, dilated the vagina, catheterized 50 cc. of urine and irrigated the bladder with 100 cc. of 1 per cent silver nitrate solution in water for 5 minutes. Washed bladder with 50 cc. of water immediately after.

5-29-'12. Animal weighs 11.3 kilos (25 lbs.); is not very active but in good condition otherwise. Gave 700 cc. of water by stomach tube. Diuretic time 45 minutes. Washed bladder as described, and collected urine.

5-30-'12. Gave 300 cc. of water by stomach tube and washed bladder in usual manner. 5 cc. of urine collected at end of 12 minutes after washing, and 11 cc. additional at end of 15 minutes.

6-10-'12. Animal normal and urine negative.

Summary, Dog C-80.—This experiment is of considerable interest in several respects. The chemical irritant (silver nitrate) assuredly caused a slight grade of cystitis, but this alone did not bring about a definite albuminuria during the period of observation. But when this irritated bladder mucosa was further stimulated by irrigation and catheterization, albumin appeared in the urine within a few minutes and in appreciable quantities. This albumin appeared during active diuresis and was obtained from a washed bladder. This prompt reaction can be explained only by some nervous reflex. In some instances, in normal dogs catheterized and irrigated for the first time, a similar reaction may occur, albumin appearing in a few minutes. It is possible that this reaction will be found to be constantly more marked when the bladder has been rendered hyper-irritable by chemical or other means.

It is worth noting, however, that in normal dogs catheterized for the first time an albuminuria may follow in a few hours or minutes. This reaction is not constant, and many or perhaps the majority of dogs do not give it. The albuminuria usually persists a few hours, but may last for a few days, and this may be dependent upon a slight cystitis induced by the catheterization.

SUMMARY.

The causation of a subacute cystitis by means of placing a foreign body in the lumen or wall of the urinary bladder is followed by an albuminuria of varying degree. The greater part of this albumin is derived from the renal secretion, as can be demonstrated by collecting urine from the ureter or from the washed bladder during diuresis. This renal albuminuria occurs in perfectly normal kidneys and may leave no trace of its occurrence in these normal organs, except the presence of hyaline casts and the resulting slight dilatation of the uriniferous tubules. Catheterization of the ureter without bladder irritation will cause no albuminuria. Chemical injury of the bladder mucosa may be associated with a reflex albuminuria, and in this irritated bladder some mechanical trauma (catheterization or irrigation) may be followed by a prompt and marked albuminuria. Further work is needed to determine whether this reflex albuminuria is found in human cases, but there is no reason to suppose these phenomena are limited to the urinary tract of the dog. It seems pretty clear that in these experiments on dogs we are dealing with a true nervous reflex in which stimuli applied to the bladder mucosa react with more or less promptness upon the renal epithelium and modify its secretory activity.

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NOTES ON NEW BOOKS.

A Text-Book of Practical Therapeutics. By Hobart Amory Hare, M. D., etc. Fourteenth Edition. (*Philadelphia and New York: Lea & Febiger, 1912*)

It is a pleasure to welcome the new edition of this excellent work, one which has proved itself eminently satisfactory to a very large number of students and general practitioners. It has grown stronger and better since it appeared first twenty-two years ago, and the profession should be grateful to the author for the careful revision he has given it. It is thoroughly reliable and most useful. We congratulate Dr. Hare on its success.

Landmarks and Surface Markings of the Human Body. By L. Bathe Rawling, M. B., B. C. (Cant.), F. R. C. S. (Eng.), etc. Illustrated. Fifth Edition. $2. (*New York: Paul B. Hoeber, 1912.*)

This small topographical anatomy is divided into five chapters covering the head and neck, the upper extremity, the thorax, the abdomen and the lower extremity. Each chapter is furnished with the plates necessary to indicate the important markings, and the text associated with the plates is so arranged by numbering each paragraph that reference between text and plate is easy. For the student whether he intends to be a surgeon or general practitioner the knowledge of such topography is all essential, and he will find this book helpful in learning his human landmarks.

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AN AID FOR THE DIAGNOSIS OF CONDITIONS ASSOCIATED WITH AN OBSTRUCTION TO THE OUTFLOW OF BLOOD FROM THE BRAIN; WITH SPECIAL REFERENCE TO SINUS THROMBOSIS OF OTITIC ORIGIN.*

By S. J. Crowe, M. D.,

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The two main pathways by which the venous blood is returned from the brain are formed by the symmetrically placed lateral sinuses, jugular bulbs, and internal jugular veins.

The main channels for a collateral circulation in case of obstruction to the outflow of blood through either of these main pathways are:

1. Through the superior and inferior petrosal sinuses to the cavernous sinus.
2. From the cavernous sinus:
   (a) To the facial vein through:
      (1) Supraorbital vein.
      (2) Superior and inferior ophthalmic veins.
   (b) To vessels of the scalp through numerous emissary veins and the sinus spheno-parietalis.
   (c) To the cavernous sinus on the opposite side by way of the sinus circularis.
3. Through the occipital sinus and posterior emissary vessels to the vertebral plexus and the external posterior jugular vein.

Thus it may be seen that there are two systems for the venous circulation in the head—one intracranial and one extracranial. These two systems are united by means of numerous anastomotic vessels; and in case there is sufficient obstruction to the outflow of blood through the intracranial system, these anastomotic vessels will become engorged with blood. At least two of these vessels, the supraorbital and ophthalmic veins, can be seen on the surface of the skin. On the other hand the retinal veins are the only branches of the intracranial venous system which can be directly observed. These vessels, however, may be studied very conveniently with the aid of an electric ophthalmoscope.

Stasis in the intracranial venous system, as may be produced by compressing both internal jugular veins, will immediately manifest itself by a dilatation of the veins of the fundi. As the stasis increases the anastomotic vessels will also begin to dilate. If the pressure on the right jugular vein is suddenly released, but that on the left is still maintained,

[1] I am indebted to Dr. Oscar Beck, assistant in the K. K. Universitäts-Ohrenklinik in Vienna, for the privilege of observing many of the cases mentioned in this paper. It was also through his kindness that the writer was permitted to assist in the operative procedures on these cases.

or vice versa, it will be observed that the distended veins in the fundi and in the skin immediately collapse and return to their normal size. This is to be explained by the fact that in normal individuals the connections between the two internal jugulars are so free, that one side alone may be occluded without producing any marked evidence of stasis. If it were otherwise one would expect to find evidence of stasis in the eye-grounds in every case of sinus thrombosis. But such is not the case. Ruttin,[2] for example, has recently reported 30 cases of sinus thrombosis in which the sinus was opened and the internal jugular vein ligated; in only 8, however, was there any evidence of choked disc. Although in 6 of these cases the choked disc did not make its appearance until after the ligation of the jugular, still there remain 22 cases in which the ligation of this vein did not produce a choked disc. We are inclined then to agree with Wagener[3] that the choked disc in cases with a sinus thrombosis is probably due to a meningitis serosa, or some other cause rather than a direct stasis of blood.

Our experience, then, has led us to conclude that any acute obstruction to the outflow of blood through the sigmoid sinus, jugular bulb or internal jugular vein on one side may be diagnosed by means of the following test. This test is based on purely mechanical principles. The anatomical conditions are schematically represented in the accompanying diagram.

From the examination of 50 normal individuals we have arrived at the following conclusions:

1. No appreciable evidence of stasis is seen in the retinal or supraorbital veins when *one internal jugular is compressed with the finger.*
2. *Pressure on both internal jugular veins at the same time* produces a marked dilatation of the veins of the fundi and of the anastomotic vessels connecting the intracranial with the extracranial venous circulation.
3. When *the pressure is suddenly released on one side, while it is maintained on the other,* the engorged veins of the anastomotic system and the fundi will immediately empty.

These are the three steps of the test which we wish to describe. If the results in any individual case differ markedly from those above, it must be concluded that there is either an anomaly of the intracranial venous circulation, or some pathological condition, which is obstructing the outflow of blood from the brain.

It is very important while making this examination that the patient should breathe freely and normally; that the collar should be loosened so as to expose the neck and upper part of the chest; and that the fundi should be examined by the direct method, or with an electric ophthalmoscope, while an assistant compresses the internal jugular veins with the tips of the fingers. The compression, however, should not be maintained longer than absolutely necessary for it may be possible in this way to rupture a diseased vein or dislodge a portion of a thrombus.

During the past two years we have had an opportunity of making this examination in 6 cases in which there was an acute obstruction, on one side, to the outflow of blood from the cranial chamber. In 5 of these cases the obstruction was due to a thrombosis, secondary to a chronic infection of the middle ear, and the test described above was employed in making the diagnosis. In 3 instances the first symptoms of the thrombosis appeared several days after the radical mastoid operation, and offered an excellent opportunity to determine the value of this sign. It is our custom to make this test before operation on all cases in which a sinus thrombosis is a possible or threatened complication. The examination of each of these 3 cases, before operation, indicated that the blood was passing freely into the internal jugular vein on both sides. This was also the opinion of the surgeon at the time of the operation, although in each case there was a cholesteatoma which extended backward to the dura of the posterior fossa. The wall of the sigmoid sinus and surrounding dura was thickened and covered with granulations. Before the operation, however, there had been no elevation of temperature, and the test had indicated that the blood was flowing freely into the internal jugular vein on both sides; therefore, it was deemed advisable to leave the sinus untouched and await developments. After a post-operative period of several days, free from discomfort or fever, the patient in each case began to complain of pain in the back of the head; there was a sudden elevation of temperature; a positive Kernig's sign; a low grade of choked disc; and some stiffness of the neck. After excluding angina, pneumonia and disturbances of the digestive tract it was necessary in each case to decide whether these symptoms were due to:

1. Serous meningitis with retention of pus in the operative wound.
2. Localized basilar meningitis.
3. Temporal lobe abscess.
4. Cerebellar abscess.
5. Sinus thrombosis.

On making the vascular test a second time it was found to be decidedly positive, *i. e.,* the stasis in the retinal and supraorbital veins was markedly increased by very slight pressure on the internal jugular vein on the healthy side, whereas at the previous examination the test had been decidedly negative. One could only conclude from this result that whatever other complications might be present, it was sure that the blood was no longer flowing freely into the internal jugular vein on the side of the operation. The sinus was immediately exposed and opened, and in each case found to be thrombosed.

In one of these cases, however, even at the second operation the sigmoid sinus was fairly normal in appearance, and on incising it there was a gush of blood. We were so sure, however, that there must be an obstruction somewhere between

[2] Ruttin: Ueber Stauungspapille bei otogenen Komplikationen. Verhandlungen der Deutschen otologischen Gesellschaft, Frankfurt-a-M., 1911.

[3] Wagener: Zur Kenntnis der intrakraniellen Komplikationen im Anschluss an Mittelohreiterungen. Passow-Schaefer Beiträge, 1911, IV, 205-256.

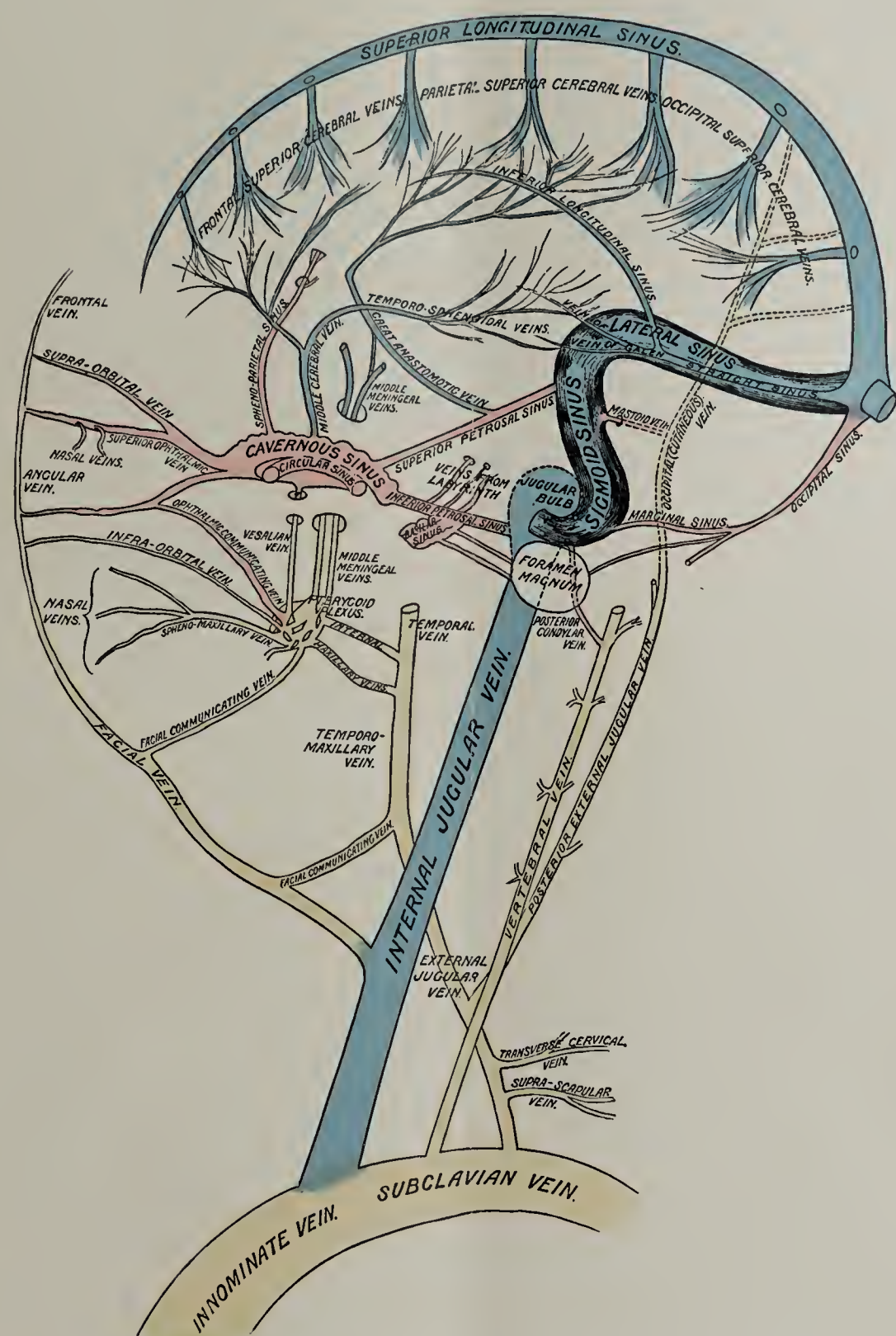

FIG. 1.—Diagram illustrating the intracranial and extracranial venous systems and their anastomotic vessels.

Blue = the intracranial venous system.
Brown = the extracranial venous system.
Red = the anastomotic vessels connecting the intracranial with the extracranial venous system.

(Modified from Macewen: Diseases of the Brain.)

this point and the innominate vein, that the cerebral end of the sinus was packed with gauze and the incision in the sinus wall enlarged downward. Then by pressure on the upper part of the internal jugular vein in the neck pus was forced upward into the wound. Further investigation disclosed a thrombus in the bulb which, however, was not purulent. Apparently this was a case of a primary abscess in the jugular fossa with a secondary thrombosis of the vessel. If we had not been certain, as a result of the positive test for stasis, that there was an obstruction to the outflow of blood into the jugular vein on this side, we should not have felt justified in opening an apparently normal sinus and exploring the bulb. Consequently the condition would not have been recognized until the peri-jugular abscess had become much larger and the chances for the patient's recovery less favorable.

The 2 remaining cases were not seen until after the operation, at which time the internal jugular vein had been ligated on one side. They are of value, however, since the test was positive in both instances, *i. e.*, light pressure on the internal jugular vein on the sound side immediately produced a dilatation of the retinal and supraorbital veins, which promptly disappeared when the pressure was released.

We have not been able to definitely determine the length of time this sign will persist after ligation of the internal jugular on one side. With this point in mind, however, we have examined 10 operated cases in which the sinus had been opened, and the internal jugular ligated, from six weeks to one year previously. In many of these cases compression of the jugular on the sound side produced no appreciable evidence of stasis, even in the retinal veins. It is our impression, therefore, that after a month or six weeks, the vessels for the collateral circulation become sufficiently large to compensate for the ligated jugular. One case, in which both sinuses had been opened and both internal jugulars ligated, by Dr. Ruttin, about fifteen months previously, was very interesting in this connection. In this man a tight bandage around the neck caused a flushing of the face, but no appreciable dilatation of the retinal veins, and but very slight subjective discomfort. This was apparently due to the fact that the collateral circulation was largely through the deep anastomotic connections with the extracranial venous system—the vertebral plexus, pterygoid plexus, etc. The fundi were also interesting. The outlines of the disc were not clear on either the temporal or the nasal side; the lamina cribrosa could not be seen on either side; and there were numerous areas of scar tissue on both retinæ, which probably represented the organization of large extravasations of blood.

Among the clinical conditions which may be associated with an obstruction to the outflow of blood from the brain, the formation of a thrombus in the sigmoid sinus, secondary to an infection of the middle ear, is by far the most frequent and the most important. Sinus thrombosis appears with equal frequency as a complication of acute and chronic cases of otitis media, and not infrequently the diagnosis offers great difficulty. Due to the anatomical position of the jugular bulb to the middle ear, it is possible to have a primary bulb thrombosis, with the sigmoid and transverse sinuses normal in appearance; and the condition may not be recognized, even at an exploratory operation. One of the cardinal symptoms of sinus thrombosis is a remittent fever with chills; due to the serious nature of the malady, however, it is desirable to know at an early stage of the disease whether the symptoms are really due to a sinus thrombosis, or to other conditions, such as: angina, pneumonia, malaria, the initial stage of one of the infectious diseases of children, meningitis or brain abscess.

As we have already stated, no normal person has as yet been observed by us in whom the compression of one jugular alone produced any marked degree of stasis in the retinal veins. On the other hand, in all normal individuals, a quite evident dilatation of these vessels results when simultaneous pressure is made on both sides of the neck. Since a sinus thrombosis offers a more or less complete obstruction to the outflow of blood into the internal jugular vein on the same side, it naturally follows that in such cases there will be unmistakable evidence of stasis as a result of compressing, with the finger, the internal jugular vein on the opposite side. When it is possible to examine a patient before the onset of complications and find that both jugular veins are patent, and at a later period, associated with an elevation of temperature, find that the blood is not passing down one side of the neck as freely as down the other, our observations have led us to believe that this sign may be taken as positive evidence that there is a sinus thrombosis.

CHLOROFORM POISONING.

RESISTANCE OF THE PIGEON, FROG AND TERRAPIN TO LATE CHLOROFORM POISONING.

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The comparative pathology of experimental chloroform poisoning offers many interesting points for investigation, and this field has not been carefully studied as yet. The few investigators (Ostertag and others) give very unsatisfactory reports of their experiments and in general state that the pathological lesions in the lower animals (birds, amphibia, etc.) are similar to the familiar lesions found in mammals. This report deals with the lesions of *late chloroform poisoning* and not the acute poisoning during anæsthesia. Particular attention was given to study of the liver. Recent publications

(Howland, Richards, Whipple, Sperry, Hurwitz) have reviewed the characteristic anatomical picture of delayed chloroform poisoning. The liver is the only organ which is seriously injured, and if the damage is severe the patient or animal dies from hepatic insufficiency. The hepatic lesion is studied to best advantage during the second day after the administration of the anæsthetic. In gross the central liver necrosis is very obvious at this time and the accompanying fatty degeneration may be conspicuous. The microscope shows a typical hyaline central necrosis of varying extent, in which areas the liver cells show pyknotic, fragmented or fading nuclei and hyaline necrotic protoplasm. The middle zone may show more or less fatty degeneration involving the liver cell protoplasm, and the marginal (portal) zone usually shows normal liver cells.

It has been shown conclusively that the common laboratory animals (dog, cat, rabbit, guinea pig, rat and mouse) react pretty constantly to chloroform anæsthesia. Two hours of surgical anæsthesia will almost certainly produce considerable central liver necrosis and fatty degeneration in these animals. The change is most conspicuous during the second day and, as a rule, this injury can be repaired rapidly and the liver brought back into a normal condition in a few days. If the injury is too severe, the symptoms become progressively more serious and the animal dies in three to five days with the familiar clinical picture.

It is also clearly established that human beings are similarly susceptible to chloroform anæsthesia, that fatal poisoning may follow less than one hour of anæsthesia and that the clinical and anatomical pictures are identical in every respect with those studied by animal experiments. It seems safe to conclude that mammals are pretty uniformly susceptible to late chloroform poisoning.

There is an interesting exception to this rule, however. In recent publications Whipple has pointed out the fact that fetuses in utero and pups during the first three weeks of life have a marked resistance to late chloroform poisoning. It seemed possible that this immunity might be explained by the "blood islands" or nests of blood-forming cells which are so conspicuous in the liver sinuses of fetuses and young pups. As these nests of nucleated red and white blood cells become less and less numerous with advancing age, one can detect a lessening of this peculiar resistance to chloroform poisoning. Surely there is a great temptation to correlate this protection of the liver cells against this poison (chloroform) with the presence of these nucleated blood cells. The mechanism of this protection is not clear.

Following this lead one might expect to find interesting differences in the reaction to chloroform anæsthesia on the part of animals with nucleated corpuscles. Below are reported the experiments in detail which go to show that in the case of the pigeon, frog and terrapin there is a very marked resistance on the part of the liver to the poisonous action of chloroform. This increased resistance is very obvious and easily established and this fact stands out clearly. Our explanation of this peculiar resistance may be quite wrong. However, it may be due to the presence of great amounts of nuclear material in the blood stream in contact with the liver-cell columns.

Chloroform, in its action upon the liver-cells, attacks the *nucleus* particularly, and the injured cell shows early nuclear degeneration or necrosis. This protective action, therefore, centers in the liver-cell nucleus and presumably is affected by the presence of other nucleated cells in great numbers in intimate association with the liver strands. These nucleated cells (red or white) never show any signs of injury due to the presence of the chloroform.

Phosphorus, in its action upon the liver-cell, attacks the *cell protoplasm,* in marked contrast to chloroform. A study of the livers in such animals will be of interest in this connection, and we hope to report on this point in the near future. Some preliminary experiments give no evidence of any marked protection against phosphorus in the case of young pups, pigeons and frogs. Phosphorus is a true hepatic poison, but of a protoplasmic type. The presence of nucleated cells in association with the liver cells gives no increased resistance against this protoplasmic poison.

Method.

The animals were placed in a glass jar (capacity 7 liters) with a fairly close-fitting cover. Chloroform vapor was introduced by forcing air through chloroform into this jar until the concentration was sufficient to produce deep surgical anæsthesia. The animal was allowed to remain in this vapor, which was renewed as occasion demanded to maintain continuous surgical anæsthesia. The extent of the anæsthesia in pigeons was determined by their eye reflexes. When the eye reflexes were absent, surgical operations could be performed with no evidence of pain. The type and extent of the respiratory movements were best observed by noting the movement of the short feathers in the anal region.

The extent of anæsthesia for the frogs was determined by a loss of the motility of the legs. The respiratory movements often ceased before motility was lost. Noting the heart pulsation was most important. The terrapin was considered under chloroform anæsthesia when mechanical stimulus of its extremities aroused no movement. The chloroform used was manufactured by Mallinckrodt (M. C. W.) "for anæsthesia." The tissues of all these animals were hardened in 10 per cent formalin for 24 hours. Frozen sections were cut and stained for fat (Herxheimer's fat stain) and with hæmatoxylin and eosin. Paraffin sections were stained by various methods.

Bird III.

Feb. 20.	Chloroform anæsthesia,	30 min.	Vomited before and after anæsthesia.
Feb. 26.	Chloroform anæsthesia,	1 hr. 45 min.	Vomited and had convulsions.
Feb. 27.	Chloroform anæsthesia,	1 hr. 45 min.	Vomited and had convulsions.
Feb. 28.	Chloroform anæsthesia,	3 hrs. 35 min.	Vomited and had convulsions.

Total anæsthesia, 7 hrs. 35 min.

Autopsy, March 1. Gross examination: On section liver shows a yellowish tinge at the edge. The other organs are normal. Microscopical section: The liver cells are normal. There is no hyaline necrosis. There are groups of mononuclear and eosinophilic cells about the portal tissues. There is no regularity of distribution of the fat globules in the liver cells.

Bird IV.

Feb. 20.	Chloroform anæsthesia,	20 min.	Vomited before anæsthesia.
Feb. 23.	Chloroform anæsthesia,	25 min.	Vomited before and after anæsthesia.
Feb. 26.	Chloroform anæsthesia,	3 hrs. 14 min.	Vomited before and after anæsthesia.
Feb. 27.	Chloroform anæsthesia,	10 min.	Vomited before and after anæsthesia.

Total anæsthesia, 4 hrs. 9 min.

Bird No. IV died under chloroform anæsthesia. It could not be revived by artificial respiration. Autopsied at once.

Autopsy, Feb. 27. Gross examination: All the organs appear normal. Microscopical section: The liver cells are normal. Fat stains show small evenly distributed fat droplets in the liver cells.

Bird V.

April 1.	Chloroform anæsthesia, 2 hrs.	Convulsions and dyspnœa.
April 2.	Chloroform anæsthesia. 3 hrs.	Very quiet.
April 3.	Chloroform anæsthesia, 2 hrs.	Vomited yellowish material.

Total anæsthesia, 7 hrs.

Autopsy, April 5. Female bird; weight 295 grams. Gross examination: All the organs look normal except the liver. The liver is small and very dark red in color. Microscopical section: The liver cells and stroma are normal. The fat stains show small globules of fat of irregular size scattered sparsely throughout in the liver cells.

The following birds were bled just before anæsthesia:

Birds VI (a, b and c).

April 2.	Bled 3 cc.	Chloroform anæsthesia, 3 hrs.	Vomited and had convulsions.
April 4.	Bled 8 cc.	Chloroform anæsthesia. 3 hrs.	Had convulsions.
April 6.	Bled 2 cc.	Chloroform anæsthesia, 3 hrs.	Very weak and easily anæsthetized.

Total anæsthesia, 9 hrs.

Autopsies, April 8. Adult birds. Gross examination: All organs are normal but anæmic. Microscopical section: The liver cells are normal. There is no hyaline necrosis. The lobules are regular. The fat stains show small fat globules evenly scattered in the liver cells.

These three birds were kept under similar conditions and given anæsthesia together for the same periods. They were autopsied at the same time and the findings were identical. There was no obvious liver injury and not the slightest evidence of any nuclear injury.

Bird VII.

May 14.	Chloroform anæsthesia, 3 hrs.	Bled 2 cc.	Vomited.
May 15.	Chloroform anæsthesia, 2 hrs. 30 min.	Bled 2 cc.	Quiet but weak.

Total anæsthesia, 5 hrs. 30 min.

Autopsy, May 15. Bird died under anæsthesia. Gross examination: Young, rather small bird. All the organs are normal except the liver which has a distinct yellow tinge. Microscopical section: The liver cells are normal except that they are filled with small vacuoles. The fat stain shows an increase of fat globules in the periphery of the liver lobule. The fat droplets are larger than those in normal tissue.

Bird VIII.

May 14.	Chloroform anæsthesia, 3 hrs.	Bled 2 cc.	Very quiet.
May 15.	Chloroform anæsthesia, 3 hrs.	Bled 2 cc.	Vomited green material.
May 16.	Chloroform anæsthesia, 3 hrs.		Convulsions.

Total anæsthesia, 9 hrs.

Autopsy, May 20. Male bird, weighed 300 grams. Gross examination: All the organs are normal. Microscopical section: The liver cells are normal, and the lobules are regular. The fat stain shows small droplets of fat scattered in the liver cells. No cell necrosis.

Bird VIII does not show as much fat in the section as does Bird VII, but Bird VIII was under chloroform anæsthesia three hours longer.

Bird I, Control.

Male bird, weight 375 grams. The bird was killed with chloroform. Autopsy showed all organs normal. Microscopical sections: The liver cells and stroma are normal. The fat stains show small irregular-sized fat droplets scattered through the liver cells in all parts of the lobules.

Bird II, Control.

Female bird, weight 340 grams. Autopsy showed all organs normal except the pancreas, which was small and nodular. Microscopical sections: The liver sections show normal tissue. Fat stains show very small, evenly distributed fat droplets in the liver lobules. The pancreas shows an advanced grade of chronic cellular pancreatitis.

Frogs X (a, b and c).

Mar. 19.	Chloroform anæsthesia, 1 hr. 25 min.	Very quiet.
Mar. 20.	Chloroform anæsthesia, 2 hrs.	Very quiet.

Total anæsthesia, 3 hrs. 25 min.

Mar. 21. X-a dead

Autopsy, March 21. Large frog. Gross examination: All organs are normal in gross. Microscopical sections: The liver cells and stroma are normal. Brownish black pigment is scattered diffusely in the liver cells.

Two other frogs (X-b and c) kept under the same conditions except that they were anæsthetized one hour longer, 4 hours and 25 minutes in all. Autopsy two days later showed normal organs in gross and microscopically.

Frog XI.

May 14.	Chloroform anæsthesia, 3 hrs.
May 15.	Chloroform anæsthesia, 3 hrs.
May 16.	Chloroform anæsthesia, 2 hrs. 30 min.

Total anæsthesia, 8 hrs. 30 min.

Autopsy, May 16. Female frog. Large size. Died while under anæsthesia and could not be revived. Gross examination: All organs were normal except the spleen, which was greatly swollen. The disease known as "red leg" was prevalent among the laboratory frogs, and this animal was suffering from this disease. Microscopical sections: The liver cells are normal. There is no evidence of hyaline necrosis. The fat stains show an increase in the number of fat droplets, especially in the pigmented areas. The pigment was increased in amount.

Frog XII.

May 14.	Chloroform anæsthesia, 3 hrs.	Quiet, no struggling.
May 15.	Chloroform anæsthesia, 3 hrs.	Quiet, no struggling.
May 16.	Chloroform anæsthesia, 3 hrs.	Sluggish.

Total anæsthesia, 9 hrs.

Autopsy, May 17. Large female frog. Gross examination: All organs are normal. Microscopical sections: The liver cells are normal and show no necrosis. The fat stains show the small fat globules in the pigmented areas, the normal picture.

Frog IX, Control.

Autopsy, May 20. Normal frog of large size. Gross examination: All the organs are normal in gross. Microscopical sections: The liver cells are normal. Clumps of blackish brown pigment are scattered among the liver cells. The fat stain shows a few small fat globules in the clumps of black pigment.

Terrapin XIV.

Mar. 20.	Chloroform anæsthesia, 2 hrs. 30 min.
Mar. 21.	Chloroform anæsthesia, 2 hrs.

Total anæsthesia, 4 hrs. 30 min.

Autopsy, March 22. Terrapin the size of a man's hand. Gross examination: Organs are normal. Microscopical sections: The liver cells are normal. The pigment is normal in amount. The fat stains show only the normal amount of fat globules.

TERRAPIN XV.

April 29.	Chloroform anæsthesia, 7 hrs.
April 30.	Chloroform anæsthesia, 7 hrs.
May 1.	Chloroform anæsthesia. 7 hrs.
May 2.	Chloroform anæsthesia, 7 hrs.
May 3.	Chloroform anæsthesia, 7 hrs.
May 4.	Chloroform anæsthesia, 7 hrs.
May 6.	Chloroform anæsthesia, 7 hrs.
May 7.	Chloroform anæsthesia, 7 hrs.
May 8.	Chloroform anæsthesia, 7 hrs.
May 10.	Chloroform anæsthesia, death
	Total anæsthesia, 63 hrs.

Terrapin No. XV died under anæsthesia.

Autopsy, May 10. Large terrapin. Gross examination: All organs normal except the liver. The liver is of lemon yellow color with pin-point black spots. Microscopical sections: The liver cells show a great increase in the number of fat vacuoles present. There is no cell necrosis, nor nuclear degeneration. The fat stains show a marked increase in fat droplets in the liver cells.

TERRAPIN XIII.

Autopsy, April 25. Small terrapin. Gross examination: All organs are normal. Microscopical sections: The liver cells are normal. Blackish pigment is scattered through the liver cells. The black pigment is found also in large clumps. The fat stains show few fat globules in the liver cells, scattered throughout the lobules.

SUMMARY.

Chloroform anæsthesia for long periods of time produces no liver necrosis in the case of the pigeon, frog and terrapin. The liver-cells of these animals, in contrast to those of mammals, have a peculiar resistance to the poisonous action of chloroform which affects particularly the cell nucleus. Fetuses and young pups show a similar but less striking resistance on the part of the liver-cells. In both instances it is conceivable that this resistance to late chloroform poisoning is due to the presence of numbers of nucleated cells in intimate association with the liver-cell columns. These nucleated cells show no evidence of any nuclear injury. Production of a moderate grade of anemia in pigeons causes no change in the resistance to chloroform. Prolonged surgical anæsthesia (chloroform) for many hours may give rise to a certain amount of fatty degeneration (terrapin) but no demonstrable cell necrosis and nuclear degeneration.

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CLINICAL AND BACTERIOLOGICAL STUDIES ON ENDOCARDITIS LENTA.*

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During the past few years the members of the medical staff in this hospital have had their attention drawn frequently to a form of endocarditis which more recent studies have tended to establish as a definite clinical entity. This type of endocarditis, which in this country has been usually known as "subacute infective endocarditis," is also designated "endocarditis lenta" by many observers, especially in Germany. The organism causing this type of endocarditis was first carefully studied by Schottmüller[1] in 1903, who gave it the name *Streptococcus viridans*. Later in 1910 he[2] proposed the name "endocarditis lenta," and laid stress upon this disease as a form of endocarditis to be sharply differentiated from the other forms either, acute or chronic, due to the ordinary *S. pyogenes*. Following Schottmüller, the work of Horder[3] and of Libman,[4] Billings[5] and Rosenow[6] in this country, has done much to clear up this subject and has greatly extended our clinical and bacteriological knowledge.

In the past year we have had, in the medical wards, five probable cases of endocarditis lenta, in three of which the presence of the *S. viridans* in the blood stream made the diagnosis certain. Interest in these cases led to an investigation of the records of the hospital in order to determine how frequent this disease has been in the past and to collect all the cases which we have had. The study of the earlier cases in the hospital has been somewhat difficult, since the attention of the observers at that time was not called particularly to this disease as an entity, and also because its bacteriology was not so well understood. In studying the histories a number of very probable cases have not been included, because the blood cultures were either negative or the organisms isolated were not described in sufficient detail to permit their identification as the *S. viridans*.

In all, there have been fifteen cases of chronic endocarditis. Of this number four gave negative blood cultures, one showed a pneumococcus, two cases were due to a streptococcus not identified definitely, and in one very interesting case reported by MacCallum and Hastings,[7] the *Micrococcus zymogenes* was isolated and described for the first time. In six cases a coccus corresponding culturally to the *S. viridans* was isolated and in this report only these six cases which are indisputable examples of this disease are included. Three of these six cases were admitted during the past year. This apparent preponderance of cases in the past year was doubtless due, in part at least, to the fact that our past experience and better knowledge of this disease at present has put us more "on the lookout," as it were, for such cases.

* From the Medical Clinic, The Johns Hopkins Hospital.

A brief résumé of the clinical course of these cases is as follows:

Case I.—Med. No. 21969. E. D., male, age 22. Admitted to the hospital on December 17, 1907.

Complaint.—Fever, pain in joints.

Family History.—Negative.

Personal History.—General health poor. Rheumatic fever in 1892 and again in 1905. In 1907 patient was told by his physician that he had "heart trouble."

Present Illness.—Began with pains in his chest and shortness of breath, which the patient first noticed in November, 1905. In the spring of 1906 he had fever, marked dyspnea and the diagnosis of endocarditis was made. He has had fever constantly since. Complains of great weakness. In August, 1907, he had a polyarthritis.

Physical Examination.—On admission the patient showed an enlarged heart, systolic bruit at apex, diastolic murmur at base. Marked anemia. No arthritis.

Blood count: R. B. C., 5,000,000; W. B. C., 16,200; Hb., 55 per cent (Sahli).

Urine: Clear, specific gravity 1022, albumen present, no red blood cells.

Blood culture on December 20, 1907, showed *S. viridans.*

On December 21, 1907, patient had a sudden right hemiplegia with aphasia.

Patient had fever constantly, irregularly, varying from 98° F. to 104° F., usually showing evening rises. No chills. He gradually grew weaker and died, after convulsions, on February 20, 1908.

Duration of illness, two years and three months.

Anatomical Diagnosis.—Acute aortic and mitral endocarditis. Acute diffuse nephritis. Acute splenic tumor. Cardiac hypertrophy and dilatation. Bronchopneumonia. Multiple infarcts in brain, spleen and kidneys.

Case II.—Med. No. 23699. E. S., female, aged 24. Admitted to hospital on February 10, 1909.

Complaint.—Pain in left leg, weakness.

Family History.—Negative.

Personal History.—Patient has never been very strong. Rheumatic fever and chorea in 1899. Marked polyuria the past year, averages eight voidings during the night.

Present Illness.—Patient has felt quite weak for three months. Two months ago began to have pain in knees and ankles. Has had fever constantly since December, 1908.

Physical Examination.—Very pale. Heart enlarged, systolic bruit at apex, diastolic murmur at base. Some swelling and redness of both ankles.

Blood count: R. B. C., 4,320,000; W. B. C., 8650; Hb., 67 per cent (Sahli).

Urine: Negative.

Blood culture on February 11, 1909, and again on February 17, 1909, showed *S. viridans.*

Temperature during stay in hospital was never very much elevated, was irregular, varying from 98° F. to 100° F.

Patient was discharged on February 18, 1909, and went home.

Case III.—Med. No. 23954. C. I., female, age 37. Admitted to hospital April 8, 1909.

Complaint.—Weakness.

Family History.—Negative.

Personal History.—Pneumonia seven years ago. No history of rheumatic fever. Has suffered from "catarrh of the throat" for many years. Five years ago she had a sudden attack of shortness of breath and palpitation of the heart.

Present Illness.—Onset in November, 1908, five months before admission, with deep pains in the muscles of the trunk. Has had fever and occasional chills since. No arthritis. She has noticed increasing shortness of breath and palpitation of the heart the past month.

Physical Examination.—Pale. Heart somewhat enlarged. Presystolic and systolic murmur at apex. Fingers clubbed. Spleen palpable.

Blood Count: R. B. C., 3,000,000; W. B. C., 10,200; Hb., 55 per cent (Sahli). Later leukocyte counts varied between 7000 and 10,000.

Urine showed constant presence of albumen and casts. No red blood cells.

Blood culture on April 10, 1909, showed *S. viridans.*

Temperature during stay in hospital was very irregular, varying between 98° F. and 103° F.

Patient was discharged on April 21, 1909.

Case IV.—Med. No. 27998. D. S., female, age 30. Admitted to hospital October 4, 1911.

Complaint.—Fever.

Family History.—Negative.

Personal History.—Patient had an attack of arthritis, probably rheumatic fever, at the age of four, in 1885. Frequent attacks of sore throat. No history of chorea.

Present Illness.—Onset three months before admission, with loss of appetite, malaise, headache, chills and irregular fever. Six weeks before admission patient's left ankle was swollen, red, hot and painful. This condition of the ankle lasted for two weeks. She has had frequent night sweats.

Physical Examination.—Pale, heart enlarged. Systolic murmur at apex. R. B. C., 3,800,000; Hb., 65 per cent (Sahli). W. B. C. on admission were 6000, varying later between 6000 and 25,500, slowly increasing during the course of the disease.

Urine showed constant presence of albumen and casts.

On October 10, 1911, there appeared a profuse crop of petechiæ over the arms and legs. October 26, 1911, patient had a sudden left hemiplegia. Following this there was a marked euphoria. Patient gradually became weaker, more and more drowsy, and died on November 20, 1911.

Temperature was irregular, fever remittent, varying between 99.5° F. and 104.2° F.

No autopsy permitted.

Total duration of illness, three months.

Case V.—Med. No. 28504. E. G., male, age 48. Admitted to hospital on January 25, 1912.

Complaint.—Loss of weight. Swelling of legs.

Family History.—Negative.

Personal History.—Patient had a severe attack of sore throat in 1887. No history of rheumatic fever. One attack of gonorrhœa.

Present Illness.—Onset about September 15, 1911, 4 months before admission. Patient felt weak, lost his appetite and shortly afterwards noticed that the tips of his fingers were swollen and painful. A few days later he began to have marked polyuria and mycturia. He has had some fever and occasional chills since October, 1911.

Physical Examination.—Emaciation, anemia, cardiac enlargement, systolic bruit at apex, clubbing of fingers. Numerous small petechiæ in conjunctiva, over the body and extremities. Spleen not palpable.

Blood count: R. B. C., 2,900,000; W. B. C., 11,800; Hb., 52 per cent (Sahli). The leukocyte count gradually increased to 23,400 two days before death. Wassermann reaction positive.

On January 31, 1912, a pleurisy with effusion developed.

S. viridans was isolated from the blood January 27, 1912 and February 2, 1912, and from the pleural effusion on January 31, 1912.

Urine had a specific gravity varying from 1009 to 1012. Albumen and casts constantly present. Numerous red and white

blood cells. Phenolsulphonephthalein excretion—10 per cent in four hours.

The patient rapidly grew weaker, marked dyspnea developed, he became drowsy and apathetic and died February 5, 1912.

Temperature very irregular, remittent, varying from 96° F. to 104° F.

Duration of illness, four months.

Anatomical Diagnosis.—Acute ulceration and vegetative mitral endocarditis, mural thrombi in right ventricle and left auricle. Infected thrombi of posterior coronary artery, multiple thrombi in branches of right pulmonary artery. Septic and healing infarcts of spleen. Healing infarcts of kidneys, acute diffuse nephritis, acute and chronic perisplenitis, acute fibrinous pleurisy, acute splenic tumor.

Case VI.—Med. No. 82534. E. B., male, age 21. Admitted to hospital on March 27, 1912.

Complaint.—Pain about the heart, tender joints, stuttering.

Family History.—Negative.

Personal History.—Scarlet fever as a child. Frequent attacks of tonsillitis. Has had some palpitation of the heart the past two years. No history of rheumatic fever. His physician told him seven years ago that he had "heart trouble."

Present Illness.—On February 21, 1912, patient noticed a swelling of the left ankle and that the tip of his left ring finger was swollen and red. Soon afterwards a painful lump appeared above the right knee, then a round red spot on the back of the right wrist. One week later there appeared a swelling with tenderness of the right ring finger tip. Fever and chilly sensations since onset of illness. Four days before admission the patient had a sudden attack of stuttering which still persists.

Physical Examination.—Pallor, increased cardiac dullness, systolic murmur at apex. Dicrotic pulse. Clubbed fingers.

Blood count: R. B. C., 4,464,000; W. B. C., 25,500; Hb., 65 per cent (Sahli).

The leukocyte count varied between 15,000 and 28,000. Wassermann negative.

Urine: Albumen and casts constantly present, at times many red blood cells.

Blood cultures taken on March 29, 1912 and on May 1, 1912, showed *S. viridans.*

Patient gradually grew weaker, temperature irregular, varying from 98° F. to 104° F. On May 1, 1912, patient developed a sudden right hemiplegia with aphasia, which persisted until his death on May 28, 1912.

Anatomical Diagnosis.—Subacute infective endocarditis of mitral valve and wall of left auricle. Acute and chronic myocarditis. Recent and organizing infarctions of spleen and kidneys. Acute diffuse nephritis. Emaciation. Chronic adhesive pleuritis (left).

Duration of illness, 3 months.

The clinical course of all these cases shows, as do the cases reported in the literature, a remarkable similarity. Few diseases, in fact, present a more constant stereotyped picture. The onset is usually insidious, the symptoms so vague at the beginning that the patient is unable to say just when his illness began. There is often a gradually developing shortness of breath, a sense of lassitude which increases until the patient takes to his bed, accompanied by some elevation of temperature and vague pains in the joints. Painful red swelling of the finger tips, which is emphasized by Osler[8] as of great diagnostic importance, was an early sign in two cases.

The anemia, usually of a secondary type, was well marked in our cases, the hemoglobin readings varying between 50 per cent and 67 per cent (Sahli). Most of the patients have at some time during admission shown a leukocytosis varying from 10,000 to 28,000, although one case showed only 8650 and in another case the white cell count fell at times as low as 6000.

Well defined heart murmurs were constantly present in the cases of this series. All of the six cases showed involvement of the mitral valve; two of the cases had in addition an aortic lesion.*

Later in the course of the disease evidences of embolism became apparent, such as petechiæ on the skin, cerebral emboli with hemiplegia and aphasia, and emboli to the kidneys producing acute nephritis, occasionally with hæmaturia. Four of the six cases showed evidences of cerebral embolism. This complication was present in five of the eight cases reported by Lenhartz,[9] in three of the ten cases reported by Osler[l.c.] and in twenty-two of one hundred and fifty cases of endocarditis studied by Horder.[l.c.] All of the cases except one gave evidence of nephritis during life and the three cases which came to autopsy showed an acute diffuse nephritis. In two cases polyuria was one of the earliest and most constant symptoms.

Case V was of some interest in showing a pleurisy with effusion during its course. The aspirated fluid was clear and from it a pure culture of *S. viridans* was isolated.

The importance of a previous history of rheumatic fever in these cases has been emphasized by many observers. In this series, three of the six cases gave a history of an old rheumatic fever and the three cases which gave a negative history had suffered from frequent attacks of tonsillitis.

The duration of the illness in all of our cases was long, varying from three months to two years, the average duration being seven months.

All of these cases of endocarditis lenta which we have been able to follow died. This also agrees with the experience of Libman, who has found the disease invariably fatal when the presence of the organisms in the blood stream has been demonstrated. Lenhartz[l.c.] reports the recovery of one patient who, however, died later from her old *Herzleiden.* Jochmann[10] also reports two recoveries. Lorey[11] has recently reported a very interesting case with a sudden onset in which the *S. viridans* was obtained from the blood culture. This patient, after remaining in the hospital for four months, was discharged as recovered and three months later was still well. These four cases are apparently the only ones reported in which recovery took place.

The diagnosis in this disease, as has been often emphasized,

* In one probable case this year, not included in this series because of the fact that the blood cultures were constantly negative, a definite murmur was never audible. This patient ran a characteristic course for endocarditis lenta, was ill seven months and finally died several days after a cerebral embolism. An autopsy was not permitted. This patient had a rapid irregular heart, but persistent examination failed to reveal a definite heart murmur. This condition is readily explained by the tendency of the vegetations in this disease to be numerous on the walls of the heart at the base of the valves, while the lines of closure are often spared. Libman has called especial attention to this localization of the heart vegetations.

can be made positively only upon the presence of the *S. viridans* in the blood. When this organism has been isolated we can almost invariably foretell the outcome of the illness, even to prophesying the probable occurrence of cerebral embolism. It has been abundantly proved, however, that some cases of endocarditis lenta may give negative blood cultures during life, in spite of repeated attempts, although the *S. viridans* may be isolated from the heart valves after death. I have seen one such case during the past year.

In contrast to the clear-cut picture of this disease which clinical study presents to us, the bacteriological studies of the organism isolated show a very great divergence of opinion. These differences are in great measure due to the confusion which surrounds any classification of the streptococci and particularly to the difficulty with which streptococci are differentiated from pneumococci. Schottmüller, Libman, Lorey, Lenhartz and most of those who have worked with this organism, regard it as a streptococcus, while Rosenow,[l.c.] as the result of extensive studies, considers the cocccus which he has isolated from cases of chronic endocarditis to be an altered pneumococcus.

During the past few years there has been much discussion as to whether there are many strains of streptococci or whether they are all to be regarded as one single race. Marmorek[12] has championed the unitarian view and believed all streptococci to belong to one group, basing his views mainly upon the fact that one strain would produce immunity in animals against other strains. More recent studies, while confirming the close relationship which exists between streptococci as a group, have, however, shown well-marked varieties and numerous attempts at classification have been made, based upon different characteristics.

Schottmüller[1] has proposed a classification based upon difference in growth on blood-agar and distinguishes three forms:

1. *S. longus seu erysipelatos,* which produces a clear zone of hemolysis about the colonies.

2. *S. mitior seu viridans,* which grows with the production of a green pigment upon the blood-agar. This organism he considers the etiological factor in endocarditis lenta.

3. *S. mucosus,* which grows with the formation of sticky mucoid whitish colonies. This organism possesses huge capsules, ferments inulin, and is regarded by most bacteriologists as a form of pneumococcus.

Andrewes and Horder,[13] as the result of extensive studies upon some twelve hundred varieties of streptococci, distinguished four types which they classify according to variations in power of fermenting carbohydrates with acid production. Their classification is as follows:

	Milk clot.	Neutral red.	Saccharose.	Lactose.	Raffinose.	Inulin.	Salicin.	Cornelferrin.	Mannite.
S pyogenes	0	0	+	+	0	0	±	0	0
S. salivarius	+	±	+	+	±	0	0	0	0
S anginosus	+	±	+	+	0	0	0	0	0
S. fecalis	+	+	+	+	0	0	+	+	+
Pneumococcus	±	0	+	+	±	±	0	0	0

Further work upon this subject by Ainley Walker,[14] Beattie[15] and others has cast some doubt upon the value of these tests, since they have shown marked differences in the ability of the same streptococcus to ferment certain sugars when cultivated over long periods of time. Winslow[16] believes these tests to be of considerable importance in differentiating between intestinal streptococci of man, the horse and the cow, and Ainley Walker states that "it is not denied that the reactions may often yield very useful evidence as to the natural or recent habitat" of streptococci.

We have studied our cultures along both lines and have also endeavored to find, if possible, whether these organisms are modified pneumococci, such as those described by Rosenow. For this work the three cultures obtained from patients Nos. IV, V and VI have been used, one culture obtained outside and a fifth culture kindly sent by Dr. Ladd of Cleveland, who isolated it from the blood of a patient with endocarditis. All of these organisms have shown a great similarity in their cultural reactions.

The organisms, when first isolated in blood cultures, grew very feebly, appearing on the blood-agar only after 48 hours, and in one case only after six days. On the blood-agar plates they grew with the production of a definite greenish pigment, when viewed by direct light and surrounded by a very slight clear zone of hemolysis in marked contrast to the wide zone of hemolysis produced by the *S. pyogenes.* This production of green has also been constant in subcultures when the organisms are grown at varying levels throughout a blood-agar plate, while if simply inoculated upon the surface, the colonies are frequently whitish and show no tendency to form the greenish pigment. The intensity of the green also seems dependent in part upon the amount of blood in the medium.

The organism grows as a very small coccus which is Gram positive, shows no capsules and produces, as a rule, long chains varying from ten to twenty cocci in length on an average. In broth the coccus grows with the production of a granular deposit at the bottom of the flask, although after being grown upon artificial medium, it often produces a diffuse turbidity. In glucose broth it grows very luxuriantly. In litmus milk, acid and clotting were produced in 24 to 48 hours by all the cultures except one, which was isolated from patient No. IV, and has never produced any change, although it grows quite well in this medium. Upon serum glucose agar all of the cultures produced a marked white precipitate around the colonies. No gas was formed in glucose agar.

We have never had sufficient evidence to consider these organisms as altered pneumococci. Capsules have never been demonstrated in any of the cultures as obtained from the patient, after prolonged cultivation for ten months, in the peritoneal fluid or heart blood of animals dead from experimental infection, or in subcultures which had passed through animals.* Similarly, none of these procedures has changed its morphology or lessened its ability of form chains. One strain

* In staining for capsules we have used Welch's method and Rosenow's l. c. method. Capsulated pneumococci when incubated with normal serum for two hours show excellent capsules, easily demonstrated by Wilson's stain or gentian violet. Our cultures

which has been grown upon artificial media for ten months and passed through mice, has constantly produced, and still forms, long chains of forty or more cocci when grown in glucose broth. None of the cocci has fermented inulin when first isolated or upon subsequent subcultures and passage through mice.

Upon the serum glucose agar medium, recommended by Libman as a valuable method of distinguishing streptococci from pneumococci, the organisms, as already stated, grew with the production of a deep white precipitate in the medium. Five strains of typical pneumococci showed only a very slight, almost imperceptible clouding. These organisms have also been tested for their solubility in bile, according to the method of Neufelt,[17] and do not dissolve, while typical virulent pneumococci do.

The study of these cultures along the above lines leads us to regard them as streptococci, belonging to the *S. viridans* group of Schottmüller, and they are probably identical with the organism described by Libman as the "endocarditis coccus."

These streptococci, examined with reference to the classification of Andrewes and Horder, showed the following reactions upon the various media.

	Milk clot.	Saccharose.	Lactose.	Raffinose.	Inulin.	Salicin.	Mannite.
1	0	+	0	+	0	+	0
2	+	+	+	+	0	+	0
3	+	+	+	+	0	0	0
4	+	+	+	+	0	0	0
5	+	+	+	+	0	0	0

These tests have been repeated frequently over a period of four months and have shown no change in fermentation reactions. For these tests 1 per cent of the various substances in sugar free broth or hydrocele broth was used. The chemicals were obtained from Merck & Co. and acid fuchsin was used as an indicator. Subcultures were subsequently made in each instance from the tubes and examined, to guard against defective growth or contamination.

Except for salicin, the fermentation reactions were the same for all the organisms, with the notable exception of No. 1, which did not ferment lactose. This also, it may be remarked, is the same culture which produces no acidity or coagulation in milk, depending possibly upon this inability to attack lactose.

In classifying these cultures according to the plan of Andrewes and Horder, it is apparent that our organism is not the *S. anginosus,* which is a hemolyser. The fact that it does not produce hemolysis, forms a clot in milk and ferments raffinose, excludes it as a *S. pyogenes.* This forces it into either the *S. salivarius* or the *S. fecalis* group and it does not belong to the latter group since this is distinguished by the "arbitrary mannite test"—the ability to ferment mannite. This leaves only the *S. salivarius* group as the possible class to which it may belong. "Short chains in broth which is rendered uniformly turbid," which Andrewes and Horder state is characteristic of the *S. salivarius,* is not an apt description of the growth of our culture in broth, and none of the variants described by them corresponds to our culture No. 1.

Andrewes and Horder also state that the "distinction between it (*S. salivarius*) and *S. anginosus* rests only upon the somewhat shadowy character of length of chains and lesser virulence," which is certainly of much less importance than the fact that the *S. anginosus* like "*S. pyogenes* is markedly hemolytic."

However, without laying too much stress upon differences in fermentation powers, the organism which we are studying does belong to the non-hemolysing group of streptococci, and if we accept the fermentation of mannite as an arbitrary distinction then it belongs to the *S. salivarius* group of Andrewes and Horden.

The frequency with which these cases of endocarditis lenta give an old history of rheumatic fever and the tendency which some cases of rheumatic fever show to develop into "malignant endocarditis," suggests at once a possible relationship between the infecting agents of the two diseases and also, more strongly, the doubt whether some cases diagnosed as rheumatic fever may not really represent the initial stage of endocarditis lenta. Some of the cases of rheumatic fever which die and at autopsy show streptococci in the cardiac vegetations would present some difficulties in a differential diagnosis from endocarditis lenta. It seems very probable that the veins of acute rheumatic fever is as yet undiscovered; the cocci thus far described may very well be secondary invaders.

We have never succeeded in isolating the *Micrococcus rheumaticus* from the blood stream of any patient in this hospital suffering from rheumatic fever, although blood cultures have been made upon such cases as a routine the past few years. However, as is well known, Poynton and Paine[18] have described a coccus, the *M. rheumaticus,* obtained from the blood and joints of rheumatic patients, which they consider the specific organism. Through the kindness of Dr. Winslow (curator of the American Museum of Natural History, N. Y.) we have received three cultures supposed to be the *M. rheumaticus.* No. 254 was obtained originally from Dr. J. M. Beattie, No. 34 from Dr. Paine and No. 399 from Dr. Lentz. These organisms we have studied along the same lines as the streptococci already considered.

These organisms produce green upon blood-agar, and the colonies are surrounded by a very slight clear zone. The coccus is very minute, grows in long chains, is Gram positive, shows no marked hemolysis as does the *S. pyogenes,* coagulates milk and produces a dense white precipitate on serum glucose agar. It does not ferment inulin and is not dissolved by bile. These cultural reactions are all common to the *S. viridans* and from them no distinguishing point is seen

stained by this method have also failed to show capsules. This "incubation method" devised by Dr. Leutscher and Dr. Clough, has been used the past year in the laboratories of the Biological Division of the Medical Clinic here, with excellent results.

between the two organisms. Rosenow[l.c.] has also remarked that they show similarities.

These strains, tested by the fermentation reaction, showed the following results:

	Glucose.	Saccharose.	Lactose.	Raffinose.	Inulin.	Salicin.	Mannite.
254	+	+	+	0	0	+	+
34	+	0	+	0	0	0	0
399	+	+	+	0	0	+	+

Following the classification of Andrewes and Horder, Nos. 259 and 399 are examples of the *S. fecalis,* while No. 34 belongs to the *S. salivarius* group. This agrees with the results of these two workers, who found that the examples of the "rheumococcus" studied by them, belonged to either the *S. salivarius* or *S. fecalis* group.

The *S. viridans* is easily distinguished from the *M. zymogenes* of MacCallum and Hastings,[l.c.] which, as previously stated, was obtained from a case of chronic endocarditis in this hospital. The *M. zymogenes,* according to their description and the later studies of Harris and Longcope,[19] liquefies gelatin, produces marked peptonization of the clot formed in litmus milk and also peptonizes blood serum. We have studied a culture of the *M. zymogenes* and can confirm these striking properties of this organism, which the *S. viridans* does not possess.

The principle of complement fixation discovered by Bordet and Gengou, which has been used with such signal success in the diagnosis of syphilis and which has been employed so extensively for testing the presence of antibodies in various diseases, has not as yet been much applied in endocarditis lenta. We had an opportunity of trying this method in Case VI.

As an antigen we used cultures of *S. viridans* obtained from the patient's blood. The cocci were grown in glucose broth for 48 hours, centrifugalized, washed, emulsified in normal salt solution, heated at 60° C. for half an hour and then allowed to remain in the thermostat at 37° C. for 48 hours. Various dilutions were then made until a dilution of 1 : 3 was obtained, which was not anti-complementary. This antigen, in various dilutions from 1 : 3 to 1 : 15, was able, in the presence of inactivated serum from the patient, to fix complement completely. The serum from six other patients suffering from various diseases, used as controls, showed no fixation at all. Four of these sera showed practically no normal anti-sheep amboceptor, one of them gave a positive Wassermann reaction. These experiments were repeated three times with the same clear-cut result on each occasion.

Similarly, it was found that an antigen prepared from the ordinary *S. pyogenes,* when added to the patient's serum, would also fix complement, while an antigen prepared by the same method from a pneumococcus showed no complement fixation. There was, however, no proof that this pneumococcus antigen was a "workable antigen."

Further work along these lines may show the complement fixation test of value in diagnosing cases of endocarditis lenta with persistent negative blood cultures. Also by applying this test to animals immunized against *S. viridans, S. pyogenes* and the pneumococcus, the relationship between the three organisms may be determined more accurately. Swift,[20] working with the complement fixation method in rabbits immunized with streptococci and pneumococci, found no interreaction between the two, although there was definite interreactions between different strains of streptococci. Some of the streptococci he used correspond culturally to the *S. viridans,* and this work indicates that their relationship is closer to the streptococci than to pneumococci.

CONCLUSIONS.

The results of these studies lead to the following conclusions:

1. Endocarditis lenta, caused by the *S. viridans,* has a sufficiently distinctive picture to deserve recognition as a separate clinical entity. That cases of chronic endocarditis may also be due to the *B. influenzæ, S. pyogenes,* or pneumococcus, is, of course, well known, but such cases should be distinguished from those due to the *S. viridans,* just as epidemic cerebro-spinal meningitis, for example, is distinguished from meningitis due to the *B. tuberculosis, B. influenzæ* or *S. pyogenes.*

2. The coccus present in our cases corresponds culturally to the organism described by Schottmüller as the *S. viridans.* The most valuable method at present of differentiating this coccus from the *S. pyogenes,* is by observing the green growth on blood-agar.

This organism, following Andrewes and Horder's classification, would be considered as a *S. salivarius.* This type of non-hemolysing streptococcus, is, however, distinguished from the *S. fecalis* only by the arbitrary mannite test, one of the reactions which Ainley Walker found very inconstant in the same streptococcus when tested at long intervals. If, however, further work should prove this to be a constant difference, then it may be of some value to separate the *S. viridans* into two types.

The differences which organism No. 1 shows in not changing litmus milk or fermenting lactose, are not essential but indicate simply a "variant" of the *S. viridans* group.

3. No essential cultural differences have been noted between the *S. viridans* and the *M. rheumaticus.*

4. Complement fixation tests in one case of endocarditis lenta showed the presence in the patient's blood of specific "antibodies."

In conclusion, it is a great pleasure to thank Prof. Barker and Dr. Clough for their kind assistance and advice in preparing this report.

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THE EFFECT OF SCARLET RED ON DEFECTS IN THE MUCOUS MEMBRANE OF THE STOMACH.

AN EXPERIMENTAL STUDY.

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INTRODUCTION.

While using scarlet red * in the treatment of ulcers, of varying etiology, on the skin and on mucous membranes (in cavities where local applications could be made), it occurred to us that possibly ulcers of the alimentary tract, especially ulcers of the stomach, might be benefited by the use of scarlet red, if it could be brought into contact with the ulcerated surface.

There was no reason to believe that this dyestuff would not have a definite stimulating effect on the epithelial edges of these ulcers, as local applications of this substance to sluggish ulcers of comparable size on mucous membranes in other situations caused definite epithelial stimulation and rapid healing.

All that is necessary for the healing of such an ulcer is for healthy mucous membrane to grow across its floor and remain intact, and it seemed possible that the mucous membrane of the ulcer edges might be stimulated by the scarlet red and thus accomplish the desired result.

Proceeding on these premises it seemed wise to undertake some experimental work on animals before attempting to administer this substance to a patient suffering with gastric ulcer. With this end in view the following investigations were carried out.

Part I. Preliminary Experiments.

It was important primarily to investigate the toxicity of the substance when given internally, and also to familiarize ourselves with its effect on the general health of the animals in regard to weight, excretions, hemoglobin, etc., and for this purpose a preliminary series of experiments was carried out on dogs, and on a few rabbits.

Some of the experiments will be reported in detail, in order

* *Chemistry.*—The dyestuff used in this series was manufactured by Kalle & Company, who were good enough to furnish us with a plentiful supply for experimental purposes.

Scientific Name.—Tolueneazotolueneazo Beta naphthol.

Commercial Names.—Biebrich Scarlet R. Medicinal (Kalle & Co.); Oil Scarlet; Red B. Oil Soluble Extra-concentrated; Ponceau 3 B. ("Organic Colouring Matters," Schultz & Julius (Green), 1904, p. 108, No. 150.)

Method of Preparation.—It is made by a combination of amidoazotoluol and Beta naphthol, and has the formula,

$$C_6H_4(CH_3) - N = N - C_6H_3(CH_3) - N = N - C_{10}H_6OH \text{ (Beta)}.$$

Color.—It is a reddish brown powder, which gives a scarlet red color in oil solution. It cakes at about 175° C. and melts at 184° to 186° C., forming a dark bronze shiny mass. At about 260° C. decomposition takes place and heavy brown fumes are emitted.

Taste.—The powder and also the oil solution are tasteless.

Reaction.—A one per cent solution in neutral oil is neutral to litmus.

Solubilities.—It is insoluble in water and urine, even after boiling. It is soluble in alcohol, ether and chloroform, olive oil, fats, fatty oils, turpentine, warmed vaseline and paraffin.

One gram of finely divided powder heated gradually in 100 cubic centimeters of olive oil to 200° C. remained in solution for two days or more at ordinary room temperature. Approximately a two per cent solution can be made, but the scarlet red does not stay in solution for any length of time, and tends to precipitate at once on cooling.

A reaction which will specifically identify this dyestuff has not yet been discovered. There are, however, a number of color reactions with various acids, which we will not consider at this time.

The gastric juice, experimentally, has no effect on the scarlet red.

X-ray Findings.—This material casts no shadow on an X-ray plate.

Bactericidal Properties.—A luxuriant growth of *Bacillus coli* and also of *Staphylococcus aureus* was obtained in 24 hours from both agar and bouillon cultures intimately mixed with one per cent oil solution of scarlet red. This seems to show that this substance has little, if any, bactericidal property.

to give an idea of the experimental procedure and also to compare the different methods of administration.

Autopsy.—The conjunctivæ and mucous membranes were not stained. *The fat of the entire body was colored a rose pink.*

On opening the stomach (18 hours after the last administration), fine red oily globules were seen everywhere over the mucous membrane. Scarlet red was also present in the small intestine and ascending colon. Otherwise these appeared normal.

The thoracic duct contained a colorless fluid. The mesenteric and other lymphatic glands were not stained. The kidneys and bladder appeared normal. The gall bladder was normal, but the bile was a dark reddish amber color. The foam, after shaking, had a pinkish tinge. Ether and chloroform extracts gave a definite rose pink color. Microscopic examination of all tissues showed no organic change due to the dyestuff.

Dog. A.—*Fed with one per cent oil solution.* (Each cubic centimeter of oil contained 10 milligrams of scarlet red.) The animal was confined in a cage for the first three weeks and was then transferred to the yard.

Date.	Amount.	Remarks.
April 20, 1911.	5 cc.	Weight, 13¼ pounds. Mixed diet.
April 21, 1911.	5 cc.	Stool colored red.
April 25, 1911.	5 cc.	
April 26, 1911.	5 cc.	Urine examination, amber color, negative for blood, casts and albumin.
April 29, 1911.	.2 grams	
May 1, 1911.	5 cc.	Animal developed distemper.
May 3, 1911.	5 cc.	Profuse nasal discharge and deep cough.
May 4, 1911.	.....	Rather severe diarrhea.
May 5, 1911.	55 cc.	No vomiting.
May 6, 1911.	.....	Diarrhea continuous. Occult blood in stools. (Guiac test.) Microscopic examination negative, for red blood corpuscles.
May 8, 1911.	5 cc.	Condition improved.
May 11, 1911.	50 cc.	
May 12, 1911.	.....	Diarrhea still severe.
May 13, 1911.	5 cc.	Dog transferred to yard.
May 15, 1911.	5 cc.	
May 17 1911.	5 cc.	
May 20, 1911.	5 cc.	
May 22, 1911.	5 cc.	General condition improving.
May 23, 1911.	.....	Hard stool.
May 24, 1911.	5 cc.	
May 26, 1911.	5 cc.	
May 29, 1911.	5 cc.	Stool well formed.
May 31, 1911.	10 cc.	
June 1, 1911.	5 cc.	
June 3, 1911.	10 cc.	
June 5, 1911.	5 cc.	
June 7, 1911.	5 grams scarlet red in oil emulsion.	Animal vomited almost all of the emulsion.
June 9, 1911.	5 cc.	
June 13, 1911.	10 cc.	
June 16 1911.	10 cc.	
June 17, 1911.	20 cc.	
June 20, 1911.	10 cc.	
June 22, 1911.	15 cc.	Hard stools. Hemoglobin, 92 per cent. (Sahli.)
June 23, 1911.	15 cc.	
June 24, 1911.	10 cc.	
June 27, 1911.	20 cc.	Stools oily and colored red throughout the treatment.
June 28, 1911.	.....	9.30 a. m. Animal sacrificed. Weight, 13½ pounds. (Gain of ¼ pound.) General condition excellent. During the treatment the animal was given a little over 3.5 grams of scarlet red, exclusive of that vomited.
Total	325 cc.	

Comment.—This animal was given doses of one per cent scarlet red in olive oil for nearly ten weeks. The doses varied between 5 cubic centimeters and 55 cubic centimeters. The amount of scarlet red given was 3.5 grams. There was a gain of ¼ pound in spite of the fact that the animal developed a severe attack of distemper five days after the feeding began. Diarrhea commenced shortly after this and was undoubtedly due to the distemper, as it lasted during the attack and then on recovery promptly ceased, although the doses of the oil averaged larger during the latter part of the experiment.

The urine was not colored red and on several occasions examination was negative for blood, casts and albumin. The stools became red about 24 hours after the first dose of oil solution. Occult blood was found in the stools (Guiac test), but no red blood cells microscopically. This can be accounted for by the mixed diet.

In addition to the one per cent oil solution .2 grams of the powder were given in a capsule, and at another time an emulsion of 5 grams of the powder in oil, but this emulsion was vomited. There was no other vomiting noted.

Following the oil feeding the fat over the entire body was stained a rose pink. The coloring matter could also be demonstrated in the bile.

Dog B.—*Fed with dry powder.* The animal was confined in a cage throughout the treatment.

Date.	Amount.	Remarks.
April 25, 1911.	.6 gm, in capsules.	Mixed diet. Weight, 18 pounds.
April 26, 1911.	.....	Portion of stool colored a very light pink in the morning. Another in the evening, 24 hours after feeding, definitely red. Occult blood (Guiac test) otherwise negative.
April 27, 1911.	1.5 gm.	Urine examination negative.
April 29, 1911.	1.2 gm.	
May 1, 1911.	.8 gm.	Animal has nasal discharge.
May 3, 1911.	10 cc. oil solution.	Animal developed distemper. Deep cough, nasal discharge.
May 4, 1911.	.6 gm.	Slight diarrhea,
May 5, 1911.	.2 gm.	
May 6, 1911.	.8 gm.	Diarrhea continues.
May 8, 1911.	.4 gm.	
May 9, 1911.	.4 gm.	
May 10, 1911.	.4 gm.	
May 11, 1911.	.4 gm.	
May 12, 1911.	.4 gm.	Diarrhea continues.
May 15, 1911.	.4 gm.	
May 16, 1911.	.4 gm.	
May 17, 1911.	.2 gm	
May 20, 1911.	.2 gm.	
May 22, 1911.	.2 gm.	
May 24, 1911.	.2 gm.	Diarrhea less marked.
May 25, 1911.	.2 gm.	
May 26, 1911.	.2 gm.	
May 27, 1911.	.2 gm.	
May 29, 1911.	.2 gm.	Condition of animal has improved. Rather firm stool.
May 31, 1911.	.4 gm.	
June 1, 1911.	.2 gm.	
June 2, 1911.	.4 gm.	Distemper is worse. Severe deep cough and diarrhea.
June 3, 1911.	.4 gm.	
June 5, 1911.	.2 gm.	Milk diet, fat meat and 10 cc. olive oil.
June 7, 1911.	.5 gm.	No vomiting. Same diet continued.
June 8, 1911.	.....	Same diet continued. Animal showed no ill effects.
June 9, 1911.	.....	Same diet continued. Animal showed no ill effects.
June 13, 1911.	.4 gm.	Moderate diarrhea continues.
June 14, 1911.	.2 gm.	
June 16, 1911.	.2 gm.	
June 20, 1911.	.2 gm.	
June 22, 1911.	5.0 gm.	Hemoglobin, 77 per cent. (Sahli.)
June 23, 1911.	.....	Distemper and diarrhea continues.
June 24, 1911.	.....	Animal has the mange. Weight, 17 lbs. (One pound loss.) Which can be easily explained by distemper and mange and confinement.
June 27, 1911.	1 gm.	
June 28, 1911.	.....	Purulent discharge from nose, and mangy over the greater portion of body, with loss of hair and erosions of skin. Animal sacrificed.
Total	19.2 gm.	

Autopsy.—Conjunctivæ and mucous membranes were clear. All the tissues appeared normal. There was no apparent staining of the body fat. The thoracic duct contained a colorless fluid. The stomach, esophagus and intestines appeared normal. The contents of the large bowel appeared rather red. The bladder and gall bladder were normal. Ether and chloroform extracts of the dark amber colored bile were colorless. The foam had a yellow tinge. Microscopic examination of all the tissues showed no organic change due to the dyestuff.

Comment.—This animal was given 19.5 grams of scarlet red powder in capsules over a period of 9 weeks. The doses

varied between .2 gram and 5 grams. There was loss of weight (one pound) which was probably due to the fact that the animal developed distemper a few days after the feeding was begun, and this continued until the termination of the experiment. There was the usual accompanying diarrhea. In addition to the distemper the animal was afflicted with mange. The examination of the urine from time to time was negative. There was no vomiting throughout the treatment. The stools became red about 24 hours after the first dose was given.

In comparing this animal with the one fed with scarlet red in olive oil, it is interesting to note that although nearly six times as much scarlet red was administered—in the dry form, there was no appreciable coloring of the body fat, and no pink color could be demonstrated in the bile. Giving a fat diet in connection with a large dose of dry powder seemed to have no effect on causing the coloring of the body fat.

Dog L. Weight 13¾ pounds. Feeding began December 19, 1911. Forty-five capsules of scarlet red, each containing .4 gram, were given between that date and January 4, 1912. Two to four capsules were given each day, 19 grams in all being given. There was no vomiting or diarrhea. No change in the color of the urine. Excellent condition until January 7, when the animal became ill.

January 9, 1912. Death from pneumonia. Weight, 10½ pounds. The loss was accounted for by illness. *Autopsy.*—The subcutaneous fat was not stained. The omental fat was stained a very faint pink color and the fat around the heart was a definite pink. The other organs showed no change worthy of note. Ether extract of the bile was colorless.

Comment.—This animal was fed 19 grams of scarlet red powder in 16 days. There was no toxic effect of any kind noted, although a large amount of the dyestuff was given in a short time. There was very slight pink staining of the omental fat and definite staining of the fat around the heart, otherwise the body fat was not stained.

In addition to the above the following large single doses were tried on other dogs.

Diet.	Amount, single dose.	Vomiting.	Other toxic effects.
Mixed.....	50 cc. oil solution.	Negative.	Negative.
Mixed.....	60 cc. oil solution.	4 cc. 2 hours after administration.	Negative.
Mixed.....	100 cc. oil solution.	5 cc. 2 hours after administration.	Negative.
Mixed.....	.5 gm. powder.	Negative.	Negative.
Mixed.....	1. gm. powder.	Negative.	Negative.
Mixed.....	1.5 gm. in oil emulsion.	Negative.	Negative.
Mixed.....	2.5 gm. in oil emulsion.	Negative.	Negative.
Milk, fat meat, olive oil.	5. gm. powder.	Negative.	Negative.

Rabbit 1.—Weight, 2¾ pounds. The rabbit was fed 1.5 grams of scarlet red (dry powder) divided and put into 18 capsules. One capsule was given each day from August 14 to September 5, 1911.

The animal was given a diet of vegetables and bread and butter. There was no ill effect noted throughout the experiment, and no diarrhea. There was no loss of weight at the end of the treatment.

September 6, 1911. Animal sacrificed. *Autopsy.*—The conjunctivæ and mucous membranes were not stained. The body fat everywhere was found to be stained a remarkable brilliant pink. The bile was of a light green color. The fat of the omentum and mesenteric attachments to the stomach and small and large intestines was likewise stained a brilliant pink. The glands were slightly enlarged, but showed no stain. The kidneys, liver and rest of the viscera showed no change worthy of note.

Rabbit 2.—The animal was fed each day with 5 cubic centimeters of one per cent scarlet red oil solution from August 19 to 25, 1911, and from August 25 to 30, 1911, with 10 cubic centimeters of one per cent scarlet red oil solution. Examination of the fat one month later showed marked pink color. Animal in good condition. *No autopsy.*

Rabbit 3.—Weight, 2¾ pounds. The rabbit was fed 5.8 grams of scarlet red (dry powder) divided and put into 24 capsules, given between December 19, 1911, and January 4, 1912. The animal was in excellent condition throughout the experiment.

January 9, 1912. Weight, 4 pounds. The subcutaneous and omental fat was examined and both were found stained a deep reddish pink.

February 14. The fat was again examined. It still remained a brilliant pink with very little, if any, diminution in intensity when compared with the specimen removed on January 9.

April 9. The omental fat was again examined. The pink color was considerably less marked than at the last examination. This seems to show that the color is gradually eliminated.

July 1, 1912. Weight, 4 pounds. Animal sacrificed. *Autopsy.*—The subcutaneous and omental fat showed no pink color. This shows that the color is gradually eliminated.

Comment.—The entire body fat in rabbits was stained a brilliant pink when fed with either the oil solution of scarlet red or the dry powder. The staining was as brilliant in the animal fed with 1.5 grams as in that fed 5.8 grams. No toxic effects whatever were noted, and the animals gained in weight during the experiments. In the course of several months there was a definite clearing up of the stained fat although this decolorization was very slow.

The Effect of Scarlet Red on Intestinal and Renal Secretions.

Dog C.—Weight, 28 pounds. Before the scarlet red feeding was begun the animal was placed on a controlled meat diet for three weeks and had consistently hard stools.

May 11, 1911. *10.30 a. m.* The animal was given 100 cubic centimeters (1 gram) of one per cent oil solution by mouth. *4 p. m.* Catheterized specimen of urine, amber color, acid. No color reaction on addition of alkali and acid. No albumin, or sugar. Microscopic examination showed no casts, or red blood corpuscles, but a few epithelial cells.

May 12. *10 a. m.* Catheterized specimen of urine. Dark brownish yellow color, acid. Same note as above. Microscopic examination showed no casts or red blood corpuscles, but a few epithelial cells and white blood corpuscles. *4 p. m.* Well formed, soft red stool. No diarrhea. No mucus, blood or straining at any time after administration. Occult blood test (Guiac) positive. This can be explained by the meat diet. Microscopic examination showed no red blood corpuscles. The subsequent stools were hard and were colored red until May 15.

Dog R.—Weight, 16 pounds. Before the scarlet red feeding was begun the animal was placed on a controlled meat diet for three weeks and had consistently hard stools.

May 16, 1911. *10 a. m.* Animal given 60 cubic centimeters (.6 gram) of one per cent oil solution, by mouth. *11 a. m.* Condition good. *1 p. m.* Condition good.

May 17. *10 a. m.* Animal in good condition. Mixed 24 hours specimen of urine was negative for usual urine tests. The stool was red and oily, well formed and firm. There was no diarrhea, mucus, blood or straining. Occult blood test (Guiac) was positive. This can be explained by the meat diet. Microscopic examination showed no red blood corpuscles. The last red stool came away the morning of May 18.

Further results showing the absence of effect on the kidneys are noted below:

Amount of S. R.	Specimen.	Time.	Reaction.	Albumin.	Blood, mic. and color.	Casts.	Oxidation.	Remarks.
100 cc. 1% oil solution.	Cath.	24 hrs.	Acid.	Neg.	Neg.	Neg.	Neg.	No color reaction on addition of alkali or acid. Ether extracts colorless.
100 cc. 1% oil solution.	Cath.	Every 4 hrs. for 24 hrs.	Acid.	Trace.	Neg.	Neg.	Neg.	Do
2.5 gm. S. R. in oil emulsion.	Mixed.	24 hrs.	Acid.	Neg.	Neg.	Neg.	Neg.	Do
20 cc. oil subcutaneously.	Mixed.	24 hrs.	Acid	Neg.	Neg.	Neg.	Neg	Do
30 cc. oil intraperitoneally.	Mixed.	24 hrs.	Acid.	Trace.	Neg.	Neg.	Neg.	Do

Comment.—Scarlet red seems to have no purgative effect whatever and causes no appreciable change in the action of the kidneys.

Remarks.—The foregoing experiments lead us to believe that the internal administration of scarlet red, either in oil solution or as dry powder, has no toxic effect, either on the economy as a whole, or on any special organ. There was no purgative action, and the urine was unchanged. There was no abnormal stimulation of the mucosa anywhere in the alimentary tract. The mucous membranes of the bladder and gall bladder were unaffected. Microscopic examination of the various organs and tissues showed no change which could in any way be traced to the dyestuff.

In order to determine the toxic effect of scarlet red in the lax subcutaneous tissue and in the peritoneal cavity the following experiments were made.

The Effect of Subcutaneous Injections.

Dog K. May 17, 1911. Animal given, subcutaneously through a needle, 20 cubic centimeters of sterilized one per cent oil solution.

May 18. Site of injection slightly swollen. No signs of inflammation. Urine and feces negative. Condition good. No signs of toxicity.

May 19. Condition good. The swelling at site of injection has disappeared.

May 22. What appeared to be a proliferation of the epithelium in the form of a papillary projection was seen at the site of the injection.

June 1. Animal sacrificed. *Autopsy.*—The loose subcutaneous tissue over a large area (size of hand), was found to be stained a bright red color. Free red oil seemed to lie between the tissue layers and came off readily on the hands and knife. The skin over this area was not affected. The muscles beneath were unchanged. No inflammatory exudate was anywhere found. No ulceration at site of the injection. Microscopic examination showed no inflammation.

Dog S.—Weight, 11½ pounds. February 27, 1912. *Operation.*—A small incision was made on each side of the mid-line of the back, and into each was injected 10 cubic centimeters (.3 gram), of a sterilized oil emulsion of scarlet red. The wounds were closed in two layers. There was no toxic effect following the operation, and no signs of inflammation.

March 28. Animal sacrificed. *Autopsy.*—In the subcutaneous tissue on each side of the back was an area about the size of the palm of the hand which was stained a brilliant red. There were pockets of free red oil between the tissue layers, and the staining of the fat was only local and by contact. The skin above and the muscles beneath were unaffected. There was no other staining noted and the examination was otherwise unimportant.

Comment.—Subcutaneous injections caused no irritation. The oil solution remained in the tissue unchanged and there was little if any absorption. There was local staining of the fat which came in contact with the oil. There were no toxic symptoms manifested.

The Effect of Intraperitoneal Injections.

Dog O. May 22, 1911. Animal given, intraperitoneally through a needle, 30 cubic centimeters of sterilized one per cent oil solution.

May 23. Condition good. The urine was negative.

May 24. Animal showed nothing abnormal except thickening of the epithelium at the site of injection.

May 25. Animal appeared ill.

May 26. Condition serious. Purulent discharge from right eye. Apathetic. Walked fairly well.

May 27. Death of animal. *Autopsy.*—On opening the peritoneum the viscera were seen to be stained a bright red color. About 15 cubic centimeters of red oily fluid were readily removed from the flanks. A fibrinous exudate was found covering the omentum and portions of the visceral peritoneum. The peritoneum was plastered down to the dome of the liver by a small amount of fibrinous exudate. The peritoneum was everywhere covered with oily red fluid. No ulceration was found at the site of the peritoneal injection. All the viscera were congested, but were otherwise negative. There was no staining of fat except in the peritoneal cavity, and death was due to an acute peritonitis.

Dog C. Weight, 28 pounds. June 3, 1911. The animal was given, intraperitoneally through a needle, 10 cubic centimeters of sterilized one per cent scarlet red oil solution.

June 4-27. There were no untoward symptoms.

This animal was given in another experiment 100 cubic centimeters of oil solution, by mouth, on May 11, and 1.5 grams of scarlet red powder in oil emulsion on June 22.

June 27. Weight, 28 pounds.

June 29. Animal sacrificed. Two hours before death the animal was given 1 gram of scarlet red powder, in a capsule. *Autopsy.*—The fat over the entire body was stained a rose pink, due to scarlet red oil feedings. The mucous membranes and conjunctivæ were clear. On opening the peritoneal cavity 5 cubic centimeters of a clear yellowish fluid was found, but no free scarlet red could be seen. In the region of the spleen, and closely adherent to it, there was a mass of omentum, which on section contained numerous little pockets of oily red fluid. Altogether there was a considerable amount of the oil in these pockets, and this seemed to show that the scarlet red had been encysted like a foreign body, and that very little, if any, had been absorbed. There were several similar smaller areas scattered over the abdominal cavity. The bladder and gall bladder were normal. Ether extract of the bile was colorless. The thoracic duct contained a clear colorless fluid. The mucous membranes of the esophagus, stomach and intestines were normal. The mesenteric and other glands were not colored. The stomach contained food which was colored a rose red, and after removal of this mass the entire membrane was found to be smeared with an oily red material.

Dog M. June 20, 1911. Animal given, intraperitoneally through an abdominal incision, 10 cubic centimeters of sterilized one per cent oil solution. Death of animal in 32 hours.

Autopsy.—Showed death to be due to bilateral broncho-pneumonia. The peritoneal surface was covered everywhere with an oily fluid. No inflammatory exudate was found. The mesenteric glands showed no discoloration. There was no staining of the fat, except locally in the peritoneal cavity.

Dog N. February 27, 1912. Animal given, intraperitoneally through an abdominal incision, .8 gram of a sterilized emulsion of scarlet red in 30 cubic centimeters of olive oil.

March 19. For the first two days after the injection the animal was apathetic, and then apparently recovered perfectly and remained in excellent condition until March 18, when there was a sudden collapse. Death followed within a few hours. *Autopsy.*—The wound had healed perfectly. There was a small amount of free straw colored fluid in the peritoneal cavity. The contents of the abdominal cavity were in one compact mass, being bound together with dense adhesions, which were separated with difficulty. The entire mass was stained a brilliant red color. On separating the adhesions the scarlet red oil was found here and there in pockets, and was apparently unchanged. There were large pockets behind the liver and spleen containing 6-8 cubic centimeters of the red oil. In some places encysted masses of scarlet red were found. The body fat outside of the abdominal cavity was unstained. Except for the abdominal condition the examination was unimportant. Death was caused by general plastic peritonitis.

Comment.—Small quantities of scarlet red oil injected intraperitoneally caused no untoward symptoms, and the mixture was encysted as any other foreign body. When larger quantities of the oil or oil emulsion were injected, a general peritonitis followed. There was only local staining of the fat which came in contact with the oil. This material acted in the abdominal cavity as any other non-absorbable irritating powder would, and had no specific toxic effect.

Remarks.—Effect on General Health.—Feeding scarlet red, either in oil or dry, seemed to have no deleterious effect on the general health.

Absorption.—The absorption from the subcutaneous tissues was very slow. At the end of 30 days most of the oil injected could be found lying practically free in the subcutaneous tissues. There was very little, if any, absorption following intraperitoneal injections.

Thoracic Duct.—The receptaculum chyli of an animal who was fed 20 cubic centimeters of the oil solution one hour and a half before being sacrificed, showed a definite rose pink color. Four cubic centimeters of a pinkish milky fluid was easily obtained which immediately coagulated on exposure to the air. On allowing this to stand, minute red fat globules rose to the surface. Ether extract of this showed a pink color. No pink coloration was noted in the receptaculum chyli in any of the animals fed with the dry powder, even following an oil or fat diet.

Blood.—Ether extracts of the blood of animals fed with the oil solution or with dry powder were colorless. An animal fed for 9 weeks with daily average doses of 10 cubic centimeters of oil solution of scarlet red maintained 92 per cent hemoglobin (Sahli). This, with other observations, seemed to show that the hemoglobin was not appreciably diminished.

Muscle.—Ether extracts of heart muscle and diaphragm of dogs fed with the oil solution and also dry powder, was found to be colorless. There was no staining of the general muscular system either macroscopically or microscopically.

Glands.—The glandular system showed no coloration or change either macroscopically or microscopically.

Fat.—The body fat of both dogs and rabbits was universally stained when oil solution was used for feeding. The fat of an animal fed for 9 weeks was apparently no more deeply stained than that of animals fed for 9 days. The amount of the doses also seemed to have little effect on the intensity of the color, as apparently only a small amount of the oil solution was taken up. When dry powder was used the fat of the rabbits was universally stained, possibly a little less intensely than when the oil solution was used. On the other hand when dry powder was fed to dogs the body fat was very little stained. In some, not at all, and in others, the omental fat was a faint pinkish color, and the fat around the heart was a definite pink. This was especially noticeable when comparatively large amounts of the powder were fed in a short period of time. Microscopic examination of frozen sections of the deeply stained fat showed a diffuse pink stain with an occasional minute pink droplet between the cells. Subcutaneous injection of the oil solution, or oil emulsion, caused a staining of the subcutaneous fat immediately in the vicinity of the injected material. Intraperitoneal injection stained only the fatty tissue in the abdominal cavity where it came in contact with the oil solution. Neither of these injections caused staining of the body fat in general.

Feces and Urine.—Both the oil solution and the powder apparently passed through the intestine unchanged. Some of the oil was absorbed, from the intestine, but very little of the powder was taken up.

Throughout the experiments, even when large doses of the oil solution or dry powder was given, the animal showed no signs of diarrhea, except those which developed distemper. One of the dogs with distemper recovered, and although the feeding with the oil solution (15 cubic centimeters every other day) was kept up the animal's stools became firm and well formed. At no time were there found red blood corpuscles or mucus in the stools. The urine was unchanged throughout the experiments.

Bile.—The bile of some of the animals fed with oil solution was reddish brown in color, and, on shaking, the foam had a pinkish tinge. Ether and chloroform extracts showed a definite rose pink color.

In contrast to this, ether extracts of bile from dogs fed with dry powder showed no color.

Liver and Kidneys.—Sections showed no macroscopic or microscopic staining.

Effect on Intact Mucous Membranes.—The mucous membranes appeared normal in all the experiments. No proliferation of the mucosa of the gastro-intestinal tract was noted. The mucosa of the gall bladder and urinary bladder was unaffected.

Part II. Operative Experiments.

After a consideration of the results obtained in the preliminary experiments we concluded that the toxicity of the dyestuff used was a negligible quantity, and felt justified in proceeding with the operative experiments.

The stomach was chosen as the site of the operative defects

on account of its accessibility and also because of the prevalence of ulcers in this organ.

The question arose as to the method of producing an ulcer with a control of exactly the same size in another animal. Gastric ulcers may be produced in dogs by exhaustive bleeding and by feeding, over considerable periods of time, large doses of colon or diphtheria bacilli. It is needless to say that it was impossible to obtain ulcers having the desired requirements by the use of such methods.

It is a well known fact that defects made artificially in the gastric mucosa of dogs heal very rapidly. In spite of this we determined to make defects of the same size in both feeder and control, and to examine the specimens at varying intervals.*

Fifteen sets of experiments were done on thirty dogs. The age of the animals varied between four months and one year. Ether anesthesia was used in each experiment. All the animals were sacrificed under ether anesthesia.

Technic.—The part was shaved, washed with green soap and water, then with alcohol and ether. After the skin was thoroughly dry it was painted with tincture of iodin 2.5 per cent. The iodin solution was also freely used in the open wounds and after suture of the skin. Dry sterile gauze secured by a bandage was used wherever dressings were applied.

The selected area was outlined through a gastrotomy opening with a cutting punch, 1.5 centimeters in diameter, and this marked out portion was excised with sharp scissors. The defect in each instance was made quite close to the pylorus, and as far as possible in the same situation and of the same depth.

Catgut was used for closing the mucosa of the stomach, but everywhere else fine black silk was the suture and ligature material used.

In cutting the tissues for microscopic examination an area as close to the center of the ulcer as possible was selected.

For convenience we have divided the series into three groups. I. Those fed with the oil solution of scarlet red. II. Those fed with olive oil without scarlet red. III. Those fed with dry powder. To economize space we will report fully only one typical operation.

Group I. Those Fed with One Per Cent Scarlet Red Oil.

Experiment 1.—Female, black and brown mongrel, about 1 year old.

Operation.—May 23, 1911. The stomach was brought up through an incision to the left of the mid-line, and a portion as near the pylorus as practicable was grasped in a stomach clamp. After packing off carefully, an incision was made through the stomach wall, and the sharp cutting punch was inserted and advanced, so as to mark out the area to be denuded as close to the clamp, and, consequently, as far from the incision as possible. Then this area, which was always clearly outlined, was manipulated so as to appear in the incision, and was then excised. (The depth of tissues removed varied, in some being only the mucous membrane, and in others the punch had cut down almost to the peritoneum.) The denuded area was then cauterized thoroughly with nitrate of silver stick, and allowed to fall back into its natural position.

The mucous membrane of the stomach was closed with catgut. The clamp was removed and the stomach wall was closed with a continuous inverting stitch. The outline of the defect, which could be seen through the stomach wall, was marked out on the surface with a circular suture of black silk. The stomach was dropped back. The abdominal wall was closed in layers. Dressed with dry gauze and bandage. Condition on leaving table excellent. *Per primam* healing.

May 25. Feeding begun with one per cent scarlet red oil solution; 20 cubic centimeters given. May 26: 10 cubic centimeters. May 27: 15 cubic centimeters. May 29: 20 cubic centimeters. May 31: 20 cubic centimeters. Total, 85 cubic centimeters. Mixed diet throughout the experiment.

June 1. Distemper. Animal sacrificed. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The entire body fat was stained a rose pink. The thoracic duct contained a clear, colorless fluid. The bile was not examined. The urine was not colored. There had been no leakage from the stomach wound. On opening the stomach an unhealed ulcer 1.5 x .4 centimeters with overhanging edges was found. The floor was covered with granulation tissue. The contents of the lower portion of the small intestine and colon were colored red. The mucosa of the stomach and intestines appeared normal. There was no change made out in any of the other organs except the lung involvement due to distemper.

Experiment 1.—*Control.*—Male, black and tan mongrel, about 6 months old.

Operation.—May 23, 1911. A similar operation was performed, every detail corresponding as closely as possible to that above described. Condition on leaving the table excellent. *Per primam* healing.

June 1. Condition excellent. *Examination of specimen.*—There had been no leakage from the stomach wound. On opening the stomach an unhealed ulcer 1.3 x .5 centimeters was found. The walls rose less sharply than in the feeder and did not overhang the floor, which was of granulation tissue.

Histology.—(Dr. Sprunt.) Nine day ulcers. The scarlet red and control ulcers are approximately the same size in the sections, although the control goes somewhat deeper into the circular muscular coat.

Feeder.—The ulcer is not quite as deep as the control but the presence of an acute infection probably negatives this advantage. The floor is covered with a thick layer of polymorphonuclear leucocytes and necrotic tissue, into which there is growing from below an edematous granulation tissue, showing many polymorphonuclear leucocytes. The mucosa in all parts of the section is thick and extends out over the edge of the ulcer on each side, the redundant edges almost meeting in the mid-line. The sides of the ulcer are lined by a thin layer of epithelium, which also extends over the floor for a short distance, to a somewhat greater extent than in the control.

Control.—The sides and floor of the ulcer show very little necrotic material, but are lined by a thin layer of healthy granulation tissue. The mucosa throughout the section is thin and does not jut over the edges of the ulcer. There is a thin line of proliferating epithelium covering the sides and just beginning to extend over the floor. (Result, positive.)

Experiment 2.—Male, black and yellow hound, about 4 months old.

Operation.—June 6, 1911. Usual operation. Accidentally the sharp edge of the punch cut through the peritoneum at one point. This was turned in with a purse string suture. Condition on leaving the table excellent. *Per primam* healing.

June 8. Scarlet red oil feedings begun: 15 cubic centimeters given. June 10: 10 cubic centimeters. June 12: 15 cubic centimeters. June 13: 20 cubic centimeters. June 14: 10 cubic centimeters. June 16: 10 cubic centimeters. June 17: 20 cubic centimeters. Total, 100 cubic centimeters. Mixed diet throughout the experiment.

* We take this opportunity of expressing our thanks to Dr. T. P. Sprunt for the reports on the microscopic appearance of the ulcers, and gratefully acknowledge the aid of Dr. C. W. Rand for assisting us in carrying out the operative experiments.

June 20. Death from pneumonia. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The entire body fat was stained a rose pink. The lungs showed lobar pneumonia. The thoracic duct contained a clear colorless fluid. The bile and urine were of normal color. There had been no leakage from the stomach wound. On opening the stomach a small healed ulcer was found. The walls of the depression rose quite sharply but did not overhang the floor. There was no scarlet red in the stomach or intestines, as there had been no feeding for three days. The mucosa of the stomach and intestines appeared normal. There was no change made out in any of the other organs.

Experiment 2.—*Control.* Male, black and brown mongrel, about 1 year old.

Operation.—June 6, 1911. Usual operation. Perforation duplicated and repaired. Condition on leaving the table excellent. *Per primam* healing.

June 20. Condition excellent. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a healed ulcer was found, which was somewhat larger than that in the scarlet red animal. The walls of the ulcer shaded off gradually into the surrounding mucous membranes. This ulcer seemed definitely less advanced toward final healing than that in the feeder.

Histology.—(Dr. Sprunt.) Fourteen day ulcers. Sections are poor. In the control there is some doubt at first as to the site of the ulcer.

Feeder.—The healed ulcer is of larger extent and apparently of greater depth than in the control. The muscularis mucosa has disappeared, the submucosa shows dense granulation tissue with a considerable amount of brown pigment. The more superficial part of the circular muscle is replaced by this tissue. The mucosa covers the whole site and contains well developed, almost perfectly formed glands.

Control.—There is a large denuded area, near the surface of which is a silk suture with a considerable amount of reaction about it. There is, of course, an ulcer here, but the presence of the suture and the appearance of granulation tissue at corresponding points of the underlying coats of the stomach indicate that this is the site of the incision into the organ. Near this point there is an area without muscularis mucosæ, covered by epithelium, but with very poorly developed glands. The submucosa contains immediately beneath this point dense granulation tissue with many small round cells. The muscularis is not affected. (*Result*, positive.)

Experiment 3.—Male, white and yellow bull terrier, about 8 months old.

Operation.—June 8, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 10. Scarlet red oil feedings begun, 10 cubic centimeters given. June 12: 15 cubic centimeters. June 13: 20 cubic centimeters. June 14: 10 cubic centimeters. June 16: 10 cubic centimeters. June 17: 20 cubic centimeters. June 20: 15 cubic centimeters. June 22: 15 cubic centimeters. June 23: 10 cubic centimeters. June 24: 15 cubic centimeters. June 26: 10 cubic centimeters. *Total*, 150 cubic centimeters. Mixed diet throughout the experiment.

June 27. Animal sacrificed, 18 hours after feeding. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The entire body fat was stained a deep rose pink. The thoracic duct contained a clear colorless fluid. The bile was dark sherry color and showed a pinkish tinge in the foam, and red color in ether and chloroform extracts. The urine was not colored. There had been no leakage from the stomach wound. On opening the stomach a small healed ulcer measuring 4 x 1.5 millimeters and 2 millimeters deep was found. The mucosa forming the walls of the depression overhung the floor. The floor was puckered and of a pinkish color and seemed to be perfectly healed. There was a small amount of an oily red material smeared over the stomach mucosa, and definite scarlet red in the intestines. The mucosa of the stomach and intestines appeared normal. There was no change made out in any of the other organs.

Experiment 3.—*Control.* Female, white poodle, about 1 year old.

Operation.—June 8, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 27. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a healed ulcer 5 x 2.5 millimeters was found. The mucosa forming the walls rose less precipitously than in the feeder. The floor of the defect was more sharply defined, and was a grayish translucent color. Macroscopically the defect did not seem as perfectly healed as in the scarlet red animal.

Histology.—(Dr. Sprunt.) Nineteen day ulcers. This shows a picture similar to that in Experiment 2. Both ulcers are healed. They seem to have been of about the same size. The scarlet red ulcer is a little deeper than the control. While the difference is not as striking as in Experiment 2, the mucosa over the site of the ulceration in the scarlet red section is somewhat better formed than in the control. (*Result*, positive.)

Experiment 4.—Male, white and black pointer, about 1 year old.

Operation.—June 13, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 14. Scarlet red oil feedings begun, 10 cubic centimeters given. June 16: 10 cubic centimeters. June 17: 20 cubic centimeters. June 20: 15 cubic centimeters. June 22: 15 cubic centimeters. Total, 70 cubic centimeters. Mixed diet throughout the experiment.

June 22. Animal sacrificed, 2 hours after feeding. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The entire body fat was stained a rose pink color. There had been no leakage from the stomach wound. The thoracic duct contained a pinkish fluid. The bile and urine were of normal color. On opening the stomach a small unhealed ulcer was found with overhanging walls. There was scarlet red oil over the entire mucosa of the stomach and it was also found in the duodenum, in the sigmoid and rectum. The mucosa of the alimentary tract appeared normal. There was no change made out in any of the other organs.

Experiment 4.—*Control.* Male, yellow and white bull terrier, about 1 year old.

Operation.—June 13, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 22. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a small unhealed ulcer was found. The ulcer was slightly smaller in size than in the scarlet red animal.

Histology.—(Dr. Sprunt.) Nine day ulcers. Poor sections. Almost no difference to be noted. The mucosa edges of both jut over the ulcers unusually far. The scarlet red ulcer was somewhat deeper and perhaps has a slightly larger area of open ulcer not yet covered with epithelium. (*Result*, no difference.)

Experiment 5.—Female, black and brown mongrel about 1 year old.

Operation.—June 15, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 16. Scarlet red oil feedings begun, 15 cubic centimeters given. June 17: 20 cubic centimeters. June 20: 15 cubic centimeters. June 22: 15 cubic centimeters. June 23: 10 cubic centimeters. June 24: 15 cubic centimeters. June 26: 10 cubic centimeters. June 27: 20 cubic centimeters. Total, 120 cubic centimeters. Mixed diet throughout the experiment.

June 27. Animal sacrificed, half hour after feeding. *Autopsy.*—

Conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The entire body fat was stained a rose pink. The thoracic duct contained a clear, colorless fluid. The bile was thick and resembled tincture of iodin in color. Ether extract showed a definite rose pink color. The urine was of normal color. There had been no leakage from the stomach wound. On opening the stomach a small healed ulcer was found. It was funnel-shaped and measured 3 x 4 millimeters, and was 2 millimeters deep. The mucosa forming the walls overhung the floor. The entire surface was found to be completely covered with red oil. Scarlet red could be seen as far down as the large intestine, as the animal was given some of the oil the night before. There were many active round worms in the intestine. The mucosa of the stomach and intestines appeared normal. There was no change made out in any of the other organs.

Experiment 5.—*Control.* Male, white fox terrier, about 1 year old.

Operation.—June 15, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 27. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach an irregular unhealed ulcer, 8 x 3.5 millimeters, was found. The mucosa forming the walls did not overhang the floor as in the scarlet red animal. The floor was more sharply outlined and was covered with granulation tissue and mucus.

Histology.—(Dr. Sprunt.) Twelve day ulcers. The two ulcers seem to have been of about the same size and depth. The floor of each is formed by healthy granulation tissue which extends down to the circular muscle coat. In neither case does the mucosa hang over the edge of the ulcer. It is somewhat thicker in the scarlet red section. Epitheliation is going on rapidly over each ulcer. The thin epithelial line covers the sides and all but the middle third of the floor of the control ulcer, while the whole floor has been covered in the scarlet red section. (*Result*, positive.)

Comment.—One feeder was sacrificed on account of distemper, one died of pneumonia, three were in good health when sacrificed.

In two the feedings were commenced the day after the operation, and in three, two days after operation. In two there were five feedings, and in three there were seven, eight and eleven feedings each.

The amount of one per cent oil solution given at a feeding varied between 10 and 20 cubic centimeters. The total amounts varied between 70 and 150 cubic centimeters.

In two instances the animals were fed just before being sacrificed.

The time elapsing between operation and examination of specimen was as follows: Nine days in 2 cases; 12 days in 1; 14 days in 1, and 19 days in 1.

The entire body fat was stained in each feeder. The staining was no deeper in the animal fed 150 cubic centimeters than when 70 cubic centimeters were given.

Scarlet red was demonstrated in the bile in two instances, one where the feeding was about 20 hours before death, and one where the feeding was 18 hours before death. In one instance it was not looked for, and in two none was found, this being without doubt due to the fact that the last oil feeding for this animal was two or three days before the examination was made. There was no change in the urine noted.

The mucosa of the alimentary canal, gall bladder and urinary bladder was normal in appearance.

The macroscopic and microscopic examination of the various organs and tissues showed no change due to the dyestuff.

The mucosa forming the walls of the defect, in several of the feeders, overhung the floor of the ulcer much more than in the controls.

Two of the feeders were in bad physicial condition during the latter portion of the treatment, but in spite of this the healing of the ulcer was further advanced in both of these than in the corresponding healthy controls.

The two nine day experiments showed unhealed ulcers. In Experiment 1, after feeding with 85 cubic centimeters, the ulcer was considerably more advanced toward healing than in the control. In this experiment there were five feedings, May 25, 26, 27, 29, and 31, which were begun two days after operation. The last feeding was the day before death.

The animal received the full benefit of the 85 cubic centimeters, which were given for three consecutive days, and then every other day for two feedings.

In the other nine day ulcer (Experiment 4), there were five feedings, June 14, 16, 17, 20, and 22, which were begun the day after operation. The last feeding was two hours before death, thus the animal received the benefit of only 55 cubic centimeters of the 70 cubic centimeters given. The feedings were less regular than in the other nine day experiment, and very little difference could be noted in the appearance of the ulcer in the feeder and in the control. The difference in the advancement of healing in Experiment 1 and Experiment 4 can possibly be explained by the fact that more of the oil solution was given in Experiment 1, and the feedings were at more favorable intervals.

The twelve, fourteen and nineteen day ulcers, in the feeders, were all healed. The twelve day control was unhealed. The fourteen and nineteen day controls were healed, but the mucosa was not as well developed as in the feeders.

In summing up the results of this group there is no doubt that the animals fed with the oil solution showed more advanced healing of the ulcers in four instances than in the corresponding controls. In one instance, where 55 cubic centimeters of the oil were given, the feeder and control were equally far advanced toward healing. So, from the above, we may conclude that in four out of five experiments the epithelium of the ulcer edges was stimulated considerably more in the animals fed with the oil solution than in the controls.

Group II. Those Fed with Pure Olive Oil.

In order to determine whether the scarlet red or the olive oil caused the epithelial stimulation in the first group of experiments, a second set was undertaken, in which pure olive oil was used for the feeding. The details of the first set of experiments were duplicated as far as possible.

Experiment 6.—Female, black mongrel, about 14 months old.

Operation.—May 27, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

May 29. Feeding with pure olive oil begun. The amounts and intervals between the feedings corresponded to those in Experiment 1. Mixed diet throughout the experiment.

June 5. Animal sacrificed. *Autopsy.*—There had been no leak-

age from the stomach wound. On opening the stomach a small unhealed ulcer with overhanging edges was found.

Experiment 6.—*Control.* Male, yellow mongrel, about 7 months old.

Operation.—May 27, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 5. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach an unhealed ulcer was found. The mucosa edges did not overhang the base as markedly as in the feeder.

Histology.—(Dr. Sprunt.) Nine day ulcers. There is an ulcer in each section undergoing healing with a granulation tissue floor which involves in each case the circular muscle coat of the stomach. The ulcer in the control section is deeper and considerably larger than in the feeder. Both ulcers are infected, especially the control whose floor is covered by masses of polymorphonuclear leucocytes. The superficial portion of the granulation tissue forming the floor of the ulcer shows many widely dilated and engorged capillaries, and the interstices of the tissue are filled with polymorphonuclear leucocytes. The mucosa overhangs the edges of the ulcer a little, and the line of epithelium has grown out for a short way across the floor of the ulcer. The mucosa in the feeder overhangs the ulcer to a marked extent, with two mucosal edges almost meeting each other. The uncovered floor of the ulcer is much smaller than in the control section. The acute inflammation is less and the ulcer seems smaller in every dimension. (*Result*, healing further advanced in feeder.)

Experiment 7.—Male, yellow mongrel, about 11 months old.

Operation.—May 27, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

May 29. Feedings with pure olive oil begun. The amounts and intervals between the feedings corresponded to those in Experiment 2.

June 10. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a healed ulcer 9 x 1 millimeters was found.

Experiment 7.—Control. Male, black and white fox terrier, about 7 months old.

Operation.—May 27, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 10. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach an ulcer 5 x 2 millimeters was found, which was nearly healed.

Histology.—(Dr. Sprunt.) Fourteen day ulcers. The ulcer in neither section involves the circular muscle. It extended in each into the submucosa. In the section marked feeder, the ulcer is covered not only by epithelium but by mucosa in large part. A small area in the center is covered by a line of epithelium only. Beneath this area the granulation tissue contains a few polymorphonuclear leucocytes. In the control section the ulcer seems wider. The mucosa has extended over the edges of the ulcer, but in the center there is perhaps one-fourth of its extent uncovered by epithelium. The granulation tissue forming this portion of the floor shows quite a number of polymorphonuclear leucocytes. (*Result*, healing further advanced in the feeder.)

Experiment 8.—Female, black and brown hound, about 8 months old.

Operation.—May 28, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

May 30. Feeding with pure olive oil begun. The amounts and intervals between the feedings corresponded to those in Experiment 3.

June 16. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a small depression measuring 4 x 2 millimeters marked the site of the healed ulcer.

Experiment 8.—*Control.* Male, black mongrel, about 8 months old.

Operation.—May 28, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 16. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a small depression measuring 2 x 3 millimeters marked the site of the healed ulcer.

Histology.—(Dr. Sprunt.) Nineteen day ulcers. The ulcers in the two sections seem to have been of about equal extent and are now both healed. The scar tissue is fairly dense in each, and covered in both cases by mucosa. There is no marked difference in the control and the feeder. (*Result*, equally well healed.)

Experiment 9.—Male, white fox terrier, about 9 months old.

Operation.—May 29, 1912. Usual operation. Condition on leaving table excellent. *Per primam* healing.

May 29. Feeding with pure olive oil begun. The amounts and intervals between the feedings corresponded to those in Experiment 4.

June 6. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a small, unhealed ulcer was found.

Experiment 9.—*Control.* Female, black and brown mongrel, about 7 months old.

Operation.—May 29, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 6. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a small, apparently healed ulcer was found.

Histology.—(Dr. Sprunt.) Nine day ulcers. In the feeder section the ulcer is deeper, extending into the circular muscle coat. The mucosa overhangs each edge and a line of epithelium has grown along the sides and floor of the ulcer, but leaves about one-half its surface uncovered. This portion is covered by a layer of mucus containing many polymorphonuclear leucocytes. The granulation tissue forming the floor of the ulcer is also full of polymorphonuclear leucocytes. The ulcer in the control section seems to have involved the muscle coat less than in the other. The ulcer is completely covered by epithelium. (*Result*, healing further advanced in the control.)

Experiment 10.—Male, white and black mongrel, about 8 months old.

Operation.—May 28, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

May 29. Feeding with pure olive oil begun. The amounts and intervals between the feedings corresponded to those in Experiment 5.

June 9. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a nearly healed ulcer 2 x 4 millimeters was found.

Experiment 10.—*Control.* Female, black and white mongrel, about 5 months old.

Operation.—May 28, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

June 9. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach an unhealed ulcer 4 x 9 millimeters was found.

Histology.—(Dr. Sprunt.) Twelve day ulcers. Comparison of the two sections in this set seems hardly fair. The ulcer in the feeder section extended to the circular muscle layer, and has been almost completely covered by epithelium. The ulcer in the control section went through both muscular layers and extended to the serosa. The mucosa overhangs each edge to a considerable extent. The sides of the ulcer are lined by granulation tissue, and the floor contains mucus, many polymorphonuclear leucocytes, and eosin staining hyaline material, suggestive of necrotic tissue. There has been a remarkable proliferation of the peritoneal

cells forming a thick node opposite the ulcer, and virtually preventing its perforation. This node of cells consists of anastomosing columns of polyhedral cells with a slight tendency toward a foamy protoplasm. There are capillaries here and there between the cells. At the basal portion of the node granulation tissue may be seen extending in between the columns of cells. The picture suggests that of adrenal cortex. (*Result*, healing further advanced in the feeder.)

Comment.—All of the feeders were in good health when sacrificed. The amounts of oil and the intervals between the feedings corresponded as closely as possible to those in Group I.

The fourteen and nineteen day ulcers in the feeders were healed. Both nine day ulcers and the twelve day ulcers in the feeders were unhealed. The controls in the nineteen day and nine day (Experiment 9) ulcers were healed. The rest were unhealed.

In comparing the epithelial stimulation in the feeder in Experiment 1, with its duplicate in Experiment 6, we note that there is greater stimulation of epithelium from the edges of the ulcer in the animal fed with scarlet red oil, than in the animal fed with pure olive oil.

Experiment 2, compared with Experiment 7. The development of the mucosa was much further advanced in the animal fed with scarlet red oil than in the olive oil fed animal.

Experiment 3, compared with Experiment 8. The mucosa over the ulcer was better developed in the animal fed with the scarlet red oil, than in the olive oil fed animal.

Experiment 4, compared with Experiment 9. There was little if any difference in the extent of epithelial stimulation in these two ulcers. This condition was not unexpected in these two experiments.

Experiment 5, compared with Experiment 10. The epithelial stimulation was greater in the animal fed with scarlet red oil than in the olive oil fed animal.

In Experiments 1 and 3 the size and appearance of the control ulcers were about the same as in their duplicate controls in Experiments 6 and 8.

In Experiments 2 and 5 the controls were further advanced toward healing than in their duplicate controls in Experiments 7 and 10.

In Experiment 4 the control was not so far advanced toward healing as its duplicate control in Experiment 9.

In summing up the results in this group, we find that in three instances the feeders in the animals fed with the olive oil showed more advanced healing than in the corresponding controls. In one instance the feeder and the control were equally far advanced toward healing, and in one the control was further advanced toward healing the feeder.

Now, when we compare the advancement of healing in the feeders in Group I, with those in Group II, we find that in four out of five instances the epithelial stimulation was much more marked in the animals fed with scarlet red oil, than in those fed with pure olive oil.

Although these experiments are very few in number they seem to show that there is a definite stimulation of the epithelium of the gastric mucosa caused by the scarlet red in oil, which is not caused by the olive oil alone.

Group III. Those Fed with Dry Powder, in Capsules.

Experiment 11.—Female, black and white fox terrier, about 6 months old.

Operation.—December 28, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

December 29. Feeding with scarlet red powder begun: a.m., 1 gram; p. m., .8 gram. December 30: a. m., .8 gram; p. m., .8 gram. December 31: a. m., .8 gram. January 1, 1912: a. m., 1.6 grams. January 2: a. m., 1.6 grams; p. m., 1.6 grams. January 3: a. m., 1.6 grams; p. m., 1.6. grams. Total: 12.2 grams. Mixed diet throughout the experiment.

January 4, 1912. Death from pneumonia. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The entire body fat of this animal was stained a rose pink. This can be accounted for by the fact that 1 gram of scarlet red in oil emulsion had been given the day of operation, before the dry powder was begun. The thoracic duct contained a colorless fluid. The bile and urine were of normal color. There had been no leakage from the stomach wound. On opening the stomach a small unhealed, funnel-shaped ulcer was found. The mucosa forming the walls overhung the floor, which was of granulation tissue. There was no scarlet red in the stomach, but it was plentiful in the ileum and lower bowel. The mucosa of the stomach and intestines appeared normal. No change worthy of note was made out in any other organ or tissue.

Experiment 11.—*Control.* Male, black and white fox terrier, about 1 year old.

Operation.—December 28, 1911. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

January 4, 1912. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach an oblong unhealed ulcer was found, which was larger but not so deep, as the ulcer in the feeder, although it seemed more nearly healed. The walls of the ulcer did not overhang the floor as much as in the feeder.

Histology.—(Dr. Sprunt.) Seven day ulcers. The ulcers in the sections are of about the same size, but the scarlet red ulcer is deeper than the control, hence the comparison is not altogether fair. The control ulcer is covered almost entirely with epithelium, and there is beginning regeneration of the mucosa in the middle of the ulcer's floor. There is much mucus. In the scarlet red section new formed mucosa hangs over at both edges, but there is no growth of epithelium over the floor of the ulcer, which is formed of granulation tissue. Mitosis is not marked in either of the sections. (*Result*, negative.)

Experiment 12.—Female, black and yellow mongrel, about 1 year old. Small animal.

Operation.—January 2, 1912. Usual operation. A perforation of considerable size was accidentally made through the stomach wall by the sharp punch, and was immediately sutured. Condition on leaving the table excellent. *Per primam* healing.

January 3. Feeding with scarlet red powder begun: a. m., .9 gram; p. m., .9 gram. January 4: a. m., 1.6 grams; p. m., 1.6 grams. January 5: a. m., 1.6 grams; p. m., 1.6 grams. January 6: a. m., 1.6 grams; p. m., 1.6 grams. January 8: a. m., 2 grams; p. m., 2 grams. January 9: a. m., 2 grams; p. m., 1.6 grams. January 10: a. m., 2 grams; p. m., 1.6 grams. January 11: a. m., 1.6 grams; p. m., 1.6 grams. January 12: a. m., 1.6 grams; p. m., 1.6 grams. January 13: a. m., .8 gram; p. m., .8 gram. January 14: a. m., 1.6 grams. January 15: a. m., .8 gram; p. m., .8 gram. January 16: a. m., .8 gram; p. m., .8 gram. January 17: a. m., .8 gram; p. m., .8 gram. January 18: a.m., .8 gram; p. m., 1.6 grams. January 19: a. m., 1.6 grams; p. m., 1.6 grams. January 20: a. m., 1.6 grams; p. m., 1.6 grams. *Total*, 47.7 grams. Mixed diet throughout the treatment.

January 20. Death, from distemper. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed

no evidence of staining. There was no visible staining of the body fat. The thoracic duct contained a colorless fluid. The bile and urine were of normal color. There had been no leakage from the stomach wound. On opening the stomach a small, funnel-shaped healed ulcer with overhanging walls was found. The floor was apparently covered with mucus. The mucous membranes of the stomach and intestines were normal. Scarlet red was present everywhere in the stomach and intestines. There was no change made out in any of the other organs due to the dyestuff.

Experiment 12.—*Control.* Female, black and white mongrel, about 1 year old.

Operation.—January 2, 1912. Usual operation. No perforation was made. Condition on leaving the table excellent. *Per primam* healing.

January 20. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a shallow, healed ulcer was found, whose walls did not overhang the floor.

Histology.—(Dr. Sprunt.) Nineteen day ulcers. The comparison here is not entirely fair, since, from the sections, one would at once say that the scarlet red ulcer was of considerably greater depth originally than in the control. It extends into the muscle which under the site of ulceration is infiltrated with granulation tissue throughout most of the circular coat. The site is completely covered with epithelium, but the mucosa is thin and manifestly imperfect. The control ulcer must have been comparatively shallow. The muscle is unaffected. The muscularis mucosa is interrupted for a very short distance and beneath this the submucosa is infiltrated with very vascular granulation tissue, the capillaries of which are widely distended. The mucosa over the site of the ulcer is of about normal thickness and appearance. (*Result*, negative.)

Experiment 13.—Male, black and tan mongrel, about 4 months old.

Operation.—January 11, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

January 12. Feeding with scarlet red powder begun: a. m., 1.6 grams; p. m., 1.6 grams. January 13: a. m., .8 gram; p. m., .8 gram. January 14: a. m., .8 gram; p. m., .8 gram. January 15: a. m., .8 gram; p. m., .8 gram. January 16: a. m., .8 gram; p. m., .8 gram. January 17: a. m., .8 gram; p. m., .8 gram. January 18: a. m., .8 gram; p. m., .8 gram. January 19: a. m., 1.6 grams; p. m., 1.6 grams. January 20: a. m., 1.6 grams; p. m., 1.6 grams. January 21: a. m., 2 grams. January 22: a. m., 2 grams. *Total* 23.2 grams. Mixed diet throughout the experiment.

January 22. Animal sacrificed. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The omental fat was stained a faint rose pink. Over the stomach incision and over the heart, the fat was found to be quite deeply stained. Scarlet red was found in the stomach and in the intestines, as the dog had been fed just before being sacrificed. The thoracic duct contained a colorless fluid. The bile and urine were of normal color. There had been no leakage from the stomach wound. On opening the stomach a small deep unhealed ulcer with overhanging walls was found. The floor was covered with granulation tissue. There was considerable puckering around the defect. The mucosa of the stomach and intestines otherwise was unchanged. There was no change worthy of note in the other organs or tissues.

Experiment 13.—*Control.* Female, black and yellow mongrel, about 9 months old.

Operation.—January 11, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

January 22. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach a small, perfectly healed ulcer was found. The defect was not quite as deep as that in the feeder, and the walls did not overhang so much.

Histology.—(Dr. Sprunt.) Twelve day ulcers. In these sections the ulcers are of about the same size and depth, extending into the submucosa, which beneath the ulcer shows the usual cellular granulation tissue. Possibly the scarlet red ulcer is a little the deeper. The control ulcer is covered with epithelium, and proliferation has gone on to partial reformation of the mucosa. The scarlet red ulcer shows overhanging mucosa edges, but the floor of the ulcer is covered at the edges only, leaving a larger central portion denuded. The mucosa in the two sections is not of the same type, suggesting that the ulcers were not made at exactly corresponding points in the two stomachs. In the control the mucosa is thicker throughout, and contains many acid cells. In the scarlet red section it is thinner, composed of more simple tubular glands, with no acid cells, apparently nearer the pylorus. (*Result*, negative.)

Experiment 14.—Male, black and white fox terrier, about 1 year old.

Operation.—January 23, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

January 23. Feeding with scarlet red powder begun: a. m., 2 grams. January 24: a. m., 2 grams; p. m., 2 grams. January 25: a. m., 2 grams; p. m., 2 grams. January 26: a. m., 2 grams; p. m., 2 grams. *Total*, 14 grams. Mixed diet throughout the experiment.

January 27. Animal sacrificed. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The body fat was not stained. The thoracic duct contained a colorless fluid, and the bile and urine were of normal color. There had been no leakage from the stomach wound. On opening the stomach a small, deep, unhealed ulcer with overhanging walls was found. The floor was of granulation tissue. The mucous membranes of the stomach and intestine were normal. Scarlet red was found in the ileum and colon. There was no change made out in any of the other organs or tissues.

Experiment 14.—*Control.* Male, black and white fox terrier, about 1 year old.

Operation.—January 23, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

January 27. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach an ulcer of considerably larger size than in the feeder, was found. Its floor was infected, and was covered with an inflammatory exudate.

Histology.—(Dr. Sprunt.) Five day ulcers. The scarlet red sections show less infection, but the ulcer is deeper than in the control, going through all of the muscle and separated from the peritoneum by granulation tissue. New formed mucosa overhangs each edge. A line of epithelium lines the sides and a very small part of the base. Mitoses are more numerous than in the control. The control ulcer extends well into the muscular coat. There is conspicuous acute inflammatory exudate in the floor of the ulcer and in the submucosa around it. This extends also through the muscular coat to the peritoneum where there is an organising peritonitis. A small amount of new mucosa has formed and jutted out slightly at each edge. There is a slight growth of epithelium over the base at one end. On account of the acute infection in the control a comparison seems unfair, but perhaps the increased depth of the ulcer in the scarlet red section may tend to neutralise the acute infection in the control. (*Result*, positive.)

Experiment 15.—Male, black mongrel, about 1 year old.

Operation.—January 31, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

January 31. Feeding with scarlet red powder begun: p. m., .8 gram. February 1: a. m., 2 grams. February 2: a. m., 1.6 grams; p. m., 1.6 grams. February 3: a. m., 1.6 grams; p. m., 1.6

grams. February 5: a. m., 1.6 grams; p. m., 1.6 grams. February 6: a. m., 1.6 grams; p. m., 1.6 grams. *Total*, 15.6 grams. Mixed diet throughout the experiment.

February 7. Animal sacrificed. *Autopsy.*—The conjunctivæ and mucous membranes were not colored. The skin showed no evidence of staining. The omental fat was a very faint pink, but the body fat was not stained. The thoracic duct contained a colorless fluid, and the bile and urine were of normal color. There had been no leakage from the stomach wound. On opening the stomach a small, deep, unhealed ulcer was found. The edges overhung so as to nearly conceal the defect. The mucous membrane of the stomach and intestine was normal. Scarlet red was found in the stomach, ileum and colon. No change was made out in any of the other organs or tissues.

Experiment 15.—*Control.* Male, yellow mongrel, about 1 year old.

Operation.—January 31, 1912. Usual operation. Condition on leaving the table excellent. *Per primam* healing.

February 7. Animal sacrificed. *Autopsy.*—There had been no leakage from the stomach wound. On opening the stomach an unhealed ulcer was found, which was larger than that in the feeder. The walls did not overhang so much.

Histology.—(Dr. Sprunt.) Seven day ulcers. Feeder. The ulcer extends into the muscle, but not as deeply as in the control. The floor is formed by granulation tissue. Epithelium covers the floor of the ulcer in a thin line, except for the middle third. The mucosa is redundant on both sides almost meeting in the mid-line, over the ulcer. Mitotic figures are more numerous than in the control.

Control.—Ulcer extends into the muscular coat. The floor of the ulcer is formed by a thick mass of necrotic tissue with many polymorphonuclear leucocytes. Beneath this there is a layer of granulation tissue. The proliferating epithelium lines both sides. On the floor there is only a short strip at one end. (*Result*, positive.)

Comment.—One feeder died of pneumonia, and one of distemper. Three were in good health when sacrificed. In two the feeding was begun the day of operation, and in three the day after operation. In two there were ten feedings, and in three there were seven, twenty and thirty-three feedings each. Morning and evening feedings were resorted to in each experiment, in order to keep the scarlet red powder in the stomach over as long a period as possible.

The amount of dry powder given at a feeding varied between .6 and 2 grams. The greatest amount given in a single day was 4 grams. The total amount varied between 12.2 and 47.7 grams.

In one experiment the animal died of distemper a few hours after the last feeding. In one the animal was sacrificed two hours after feeding. In both of these scarlet red was abundant in the stomach. In three where the feeding was the evening before the examination of the specimen, no scarlet red was found in the stomach. The time elapsing between operation and examination of the specimen was as follows: Seven days in 2 cases, 5, 12, and 19 days in one each.

The entire body fat was stained in one animal, as 1 gram of the powder in oil emulsion had been given before the feeding with dry powder was commenced. In two the omental fat, and the fat around the heart, was stained a faint pink, and in two there was no staining whatever.

Scarlet red was not demonstrated in the bile in any animal fed with dry powder.

There was no change in the urine noted.

The mucosa of the alimentary canal, gall bladder, and urinary bladder was normal in appearance.

The macroscopic and microscopic examination of the various organs and tissues showed no change due to the dyestuff.

The mucosa forming the walls of the defect in all but one of the feeders overhung the floor of the ulcer much more than in the controls.

The two 7 day experiments showed unhealed ulcers. In one (Experiment 11), after feeding 12.2 grams in six days there was practically no epithelial growth over the floor of the ulcer, although the ulcer was distinctly smaller, but deeper than the control. The control was nearly covered with epithelium.

In the other 7 day ulcer (Experiment 15), after feeding 15.6 grams in six days, the epithelial growth was considerably more advanced in the feeder than in the control, and the ulcer in the feeder was smaller, but deeper, than the control.

Perhaps the difference in epithelial stimulation might be due to the fact that in Experiment 11 the health of the animal was bad after the first two days, and death followed from pneumonia.

The five day ulcer in the feeder was further advanced toward healing than the control. The twelve day ulcer in the control was healed, while the feeder was not so far advanced toward healing. The nineteen day ulcers were both healed, but the mucosa in the control was developed to a greater extent.

In summing up the results of this group of experiments it will be seen that in three out of five sets of animals the controls were further advanced toward healing than the feeders. In other words feeding with the dry dyestuff did not give the same favorable results noted in Group I, although very much more of the material was introduced into the stomach. The larger amounts seem to be more than counterbalanced by the length of time the oil solution remained in contact with the defect in the stomach mucosa.

This group again demonstrates the non-toxicity of the dyestuff, which can be noted on glancing over the amounts fed in a comparatively short time. All the animals were small, and the doses were very large when the body weight was taken into consideration.

Remarks.—In Group I (fed with scarlet red oil solution), the defects made artificially in the feeders were further advanced toward healing, than in the corresponding controls, in four out of five instances.

In Group II (fed with pure olive oil), similar defects in the feeders were further advanced, than in the corresponding controls, in three out of five instances.

Comparing the advancement of the healing in the feeders in the duplicate experiments in these two groups, we find that the epithelial stimulation was more marked in those animals fed with the scarlet red oil solution than in those fed with pure olive oil.

In Group III (fed with dry powder), similar defects in the feeders were further advanced toward healing, than in the corresponding controls, in only two out of five instances.

The lack of epithelial stimulation may be due to the fact

that the feedings were too far apart to keep the material in contact with the denuded area. This objection could be obviated by giving the doses at short intervals.

In several instances the scarlet red oil solution was found smeared over the entire mucosa of the stomach, as long as 18 hours after feeding, and this suggests that the dyestuff administered in this way might stay in contact with the mucosa continuously if given at the proper intervals.

Both the powder and the oil solution were in actual contact with the denuded surfaces in every instance where an examination was made before the dyestuff had passed on into the intestine.

The stimulating effect of scarlet red on epithelium in other situations is well authenticated, so we may at least surmise that it probably had a similar stimulating effect on the epithelium in these experiments. The best results of local use of scarlet red in hastening epithelial stimulation is obtained when it is applied in an oil solution, or in a lanolin or vaseline base, and it seems probable that the most satisfactory effects in such a situation as the stomach, would be obtained when it was given in an oily solution.

We were able to examine the subcutaneous fat of two patients, one of whom had taken internally 32 grams, and the other 63.3 grams, of the dry powder within four weeks, and there was no staining of the fat. Another patient, who had been given 66.5 grams of the powder in less than four weeks, was operated on several weeks later for another trouble, and there was no staining of the subcutaneous or omental fat.

Whether the oil solution or an oil emulsion taken internally will stain human fat, we are not, as yet, prepared to say.

The use of the oil solution in treating patients might be contraindicated on account of the staining of the fat, but there is no experimental evidence of either conjunctivæ or skin being visibly stained pink. The fact that the stain is gradually eliminated is also to be borne in mind, as, if the oil solution is found to give the best clinical results, the stain will eventually disappear from the fat.*

* In order to avoid staining the skin, bed clothes, etc., it seems advisable to administer the dyestuff in a container of some sort. We might suggest that if the powder is to be used it should be given in small doses, say 5 grains every 3 or 4 hours, in capsules, in order to keep it continuously in the stomach. If the oil solution is to be given, a flexible gelatin capsule containing 4 or 5 cubic centimeters each might be given.

In none of the experiments has there been any tendency noted to the overgrowth of mucosa of the alimentary canal, and from our experience with the stimulating effect of scarlet red on epithelium in other situations, we feel that there is no more danger of producing a malignant degeneration in an ulcerated area of the stomach, than if the ulcer were properly treated by any other method. That is, medically for a reasonable time, say about six weeks, or two months, and then, unless there is definite relief of all symptoms, the case should become surgical.

In the treatment of gastric ulcer in the human a certain amount concerning the efficacy of a method can be told by the alleviation of the symptoms, but the only way to definitely determine the beneficial action of scarlet red in the treatment of these cases is to have a series of patients with all the symptoms and signs of gastric ulcer, and who would ordinarily be passed over to the surgeon, receive this treatment for several weeks, before coming to operation.

Conclusions.

The dyestuff used in this series of experiments is not toxic and apparently has no deleterious effect on either dogs or rabbits.

When given by mouth it is a fat selecting vital stain. In the course of months the stain is gradually eliminated.

Subcutaneous and intraperitoneal injections stain only the fat in actual contact with the scarlet red oil solution.

It is difficult to say from these few operative experiments whether the scarlet red has, or has not, a definite stimulating action on the epithelium of defects in the gastric mucosa. However, the scarlet red oil solution caused a more rapid and better developed growth of epithelium in the group in which it was used, than occurred in the duplicate group where plain olive oil was used.

The results with dry powder were not so favorable experimentally, but this may have been due to the fact that the material was not continuously in contact with the denuded area.

We were unable to determine the relative effect of the scarlet red on chronic gastric ulcers, as it was impossible to produce chronic ulcers in dogs with controls of exactly the same size.

Our experiments are suggestive, and, as this dyestuff may be safely administered, we feel that it is worthy of a thorough clinical trial.

SUBLUXATION OF THE MAJOR CORNU OF THE HYOID BONE (DYSPHAGIA VALSALVIANA).

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The rarity of subluxation of the major cornu of the hyoid bone, or the infrequent diagnosis of this condition, explains why so few cases have been reported. The writer's attention was attracted to this fact when he was trying to discover cases with similar symptoms to those which a patient had who presented himself for diagnosis in the Laryngological Dispensary of The Johns Hopkins Hospital.

The patient, Dr. McC——, of Texas, stated that in 1887, when a child of seven years, he suddenly became unable to swallow. He was taken by his father to a physician who tried

in vain to get something into place in his neck which had apparently become "twisted." The longer the condition persisted the more painful were his efforts to swallow.

After two days, during which time the child remained with the physician, there was a sudden restoration of the normal condition. Repeatedly, after this, he had similar attacks in which swallowing became at first painful and then impossible. They would come on when he yawned or turned his head suddenly. Sometimes the condition would be relieved of itself, as in the first attack, and sometimes he was able to obtain relief by pulling hard on the skin in front of the sterno-mastoid muscle. At the age of twenty-three he learned to "set it" as he expressed it. He inserts his index finger into his mouth at the side and base of the tongue at a point which corresponds, when one feels on the outside, to the attachment of the major cornu of the hyoid bone to the superior cornu of the thyroid cartilage, and presses outward and forward. Something goes back into position with a distinct click. These points were determined on examination during the time in which the abnormal condition was present. As far as could be determined by a laryngoscopical examination there was no change in the larynx.

A study of the anatomical relations of the hyoid bone and of the symptomatology of eleven cases of subluxation of the major cornu of the hyoid bone, including the author's case and ten cases collected from the literature, makes it seem probable that in this case there was a loose articulation of the major cornu with the body of the hyoid bone, or a loose attachment of the tip of the major cornu to the superior horn of the thyroid, allowing greater freedom of movement of the major cornu than is normally present.

I will give only a brief description of the topographical anatomy. The hyoid bone lies in most intimate relation to the larynx above and the tongue below. It is the principal support of the tongue through its muscular and ligamentous attachments, and it is associated with all the movements of the larynx by ligaments which unite it to the thyroid cartilage. The attachment of the major cornu of the hyoid bone to the superior cornu of the thyroid cartilage through the medium of the lateral thyro-hyoid ligament may be loose or firm according to the degree of tension of this ligament. The attachment of the major cornu to the body of the hyoid, sometimes osseous in advanced age, is at other times the site of a true joint containing a synovial membrane.

Olivier D'Angers,[1] in 1837, mentioned four cases of the above condition which he had collected from the literature; the first was observed by Valsalva, in which dysphagia followed the ingestion of a hard and voluminous body, and which he attributed to the dislocation of the cartilaginous appendices of the hyoid bone. The article swallowed was a piece of meat. Valsalva reduced this dislocation by pressing with his fingers at the back of the mouth. D'Angers quotes Sauvage as naming the condition dysphagia valsalviana.

The second and third cases, reported by P. B. Molinelli,[2] are as follows:

A young student of slight build was grasped violently by the throat by a much stronger man, and, in the struggle which ensued, pressure was made on the right external part of the neck. It became at once impossible for him to swallow either liquids or solids, however hard he tried. Molinelli saw him one hour after the assault; he was in a state of extreme anxiety; a cold and abundant sweat covered his whole body; his pulse was small; he seemed in danger of imminent dissolution. However, his articulation and respiration were very little altered. No deformity was noticed in the region of the larynx, but between this organ and the right sterno-mastoid muscle, there was a tumor acutely painful to the slightest pressure.

Molinelli's treatment consisted in having the patient's head held firmly while he introduced his right index finger between the right tonsil and the base of the tongue, at the same time applying the index and middle fingers of his left hand to the outer side of the neck in the region occupied by the hyoid bone. Then with the finger in the back of the mouth, the right great cornu of the hyoid bone was pushed gradually outward while the fingers placed at the outside of the neck limited and directed this pressure. This maneuver had scarcely been executed when the patient felt relieved and was able to swallow a little water. The maneuver was immediately repeated a second and a third time, with a complete disappearance of the symptoms; the prominence between the larynx and the sterno-mastoid no longer existed and the young man was able to swallow with normal ease.

Molinelli's second case was a man fifty-two years of age, who complained of extreme difficulty in swallowing, accompanied by a great deal of anxiety. His symptoms followed directly upon a blow struck in the right anterior and superior part of the neck by a man who had a stone in his fist. Three hours later, the symptoms having persisted, Molinelli employed successfully the same means as in the first instance. In this case there was no prominence in the neck as in the preceding case, and the symptoms were also less intense.

The fourth case, which D'Angers mentions, reported by Dr. Mugna (Annali universali di medicina, Nov. and Dec., 1828), concerned a sexagenarian of "tender and weakened" body who swallowed a large piece of beef tendon which he had not properly masticated, and who, immediately thereafter, had a sensation as though his œsophagus were blocked at the entrance. He felt a continual need of swallowing, but was unable to swallow his saliva or even a drop of liquid. Each moment his anxiety increased.

Called at once, Dr. Mugna found respiration and voice free and no change in the form or appearance of the throat or exterior of the neck. An œsophageal sound was easily passed, crossing the point at which the patient felt the piece of tendon had stopped, but without relief. As the patient indicated the region of the hyoid bone as the seat of the body he felt, Mugna thought of the possibility of dislocation or "diastasis" of the cartilaginous prolongations of the hyoid bone being the cause of the dysphagia. He introduced the index and middle fingers of his right hand into the back of the mouth above the base of the tongue and imparted to the hyoid bone some dis-

placing movements, while he kept his left hand in front of the neck and upon the hyoid bone. This very simple maneuver caused the painful sensation which the patient experienced to disappear immediately, and at once he was able to swallow and drink abundantly.

Two years later Dr. Mugna treated the same patient successfully, in the same manner, for a similar attack.

D'Angers differentiated two ways in which dislocation might occur, one occurring from pressure from the outside and one from pressure from within. The first one corresponds to the dislocation caused by choking as in Molinelli's first case, the second to the dislocation caused by swallowing a large body (Valsalva's case). In the first way he considered the greater cornu to be displaced inwards, its articular facet leaving more or less completely the corresponding facet of the body of the bone. He explains the effect of swallowing a voluminous body as resulting from a lateral and downward movement of the larynx, so that one of its horns engages inside of the corresponding superior horn of the thyroid cartilage, and stays maintained in this position. He thought it conceivable that pressure inwards and downwards upon both greater cornua might cause both cornua to engage in the space between the superior horns of the thyroid cartilage.

Gibb,[3] in 1859, reported a case in a man forty-five years of age, who would feel a sudden click in the left side of his neck which produced a sensation as though something were sticking in his throat. On examination this seemed to depend upon a displacement of the left horn of the hyoid bone, and was generally reduced by throwing the head backwards toward the right side so as to stretch the muscles of the neck and then suddenly depressing the lower jaw, thus putting the depressors of the hyoid bone into operation.

At the patient's death, of pulmonary tuberculosis some years after, Dr. Gibb found "a sort of pouch which answered the purpose of a synovial capsule, and embraced the left thyrohyoid articulation. It was filled with the clear fluid and had a comparatively large rhomboid sesamoid bone developed in the outer wall and permitted an extraordinary amount of motion."

Dr. Gibb had previously seen three other cases with similar symptoms, all occurring in males, and he thought probably not dependent on such an hydrarthrosis. Later he saw a fifth case in which the patient was a female.

Dr. Ripley,[4] of South Carolina, read, in 1848, before the Parisian Medical Society, a paper on dislocations of the hyoid bone, especially illustrated in his own person, and on the manner of producing them. Dr. Ripley's method of reduction consisted in throwing his head backwards as far as possible so as to place the muscles of his neck on the stretch, and relaxing the lower jaw, at the same time gently pressing or rubbing over the displaced part, "when the displacement became reduced, after a few attempts, with a click."

In 1880 W. H. Daly,[5] of Pittsburgh, reported the case of another physician, Dr. C. D. A., who had been under his treatment. The patient sought relief from a luxation of the left cornu of the hyoid bone which had occurred one-half hour before while laughing. Laryngoscopic examination was negative. The patient's head was bent forward a little to the left side. He complained of dull, pricking pain over the left cornu on straightening his neck. The patient had frequently suffered from similar attacks. His wife was in the habit of cautioning him when laughing or yawning "to take care lest he should put his neck out of joint again!"

The following method of reduction was successful after the third effort: The throat was grasped firmly below the hyoid bone with thumb and index finger of the right hand, the patient's head being steadied with the left. The patient was told to swallow vigorously. As the patient swallowed, Dr. Daley made compression and quick release of the parts between the thumb and finger.

Westmoreland's[6] first case, a policeman, aged 28, while stretching and yawning after breakfast, felt a sudden and severe pain in the side of his neck. He could not close his mouth without pain. "There was a lump over the left side of the neck just over the greater cornu. This appeared to be caused as much by the contraction of the muscles as by the displacement of the cornu." The displacement was apparently upwards and outwards. Laryngoscopic examination revealed no abnormality of either the larynx or pharynx. The patient continually complained of feeling something sticking in his throat.

"The dislocation was easily reduced by having the patient throw his head backward toward the opposite side, rubbing, pressing over the hyoid bone, and at the same time suddenly depressing the lower jaw. It was reduced with a click, audible to everyone in the room, and there was an immediate cessation of all pain."

While the patient had had similar attacks three or four times before, the first time while singing, this last attack was decidedly the worst. He had generally obtained sudden relief by rubbing his throat and moving his head backward and forward, seeking an easy position. He had consulted physicians, but without relief.

Westmoreland's second case, a young traveling salesman, complained of having been in considerable pain for three days; he was unable to keep his mouth closed without increase of pain. Talking also made his suffering worse.

Examination showed a lump over the right side of the hyoid bone, with displacement in the same direction as in the first case but less in degree. The same manipulation to aid reduction was used with success at the first trial, reduction taking place with an audible click.

This patient had also had several attacks. Physicians to whom he had applied for help had invariably prescribed gargles. While gargling with head thrown back and mouth open he would immediately or later get relief in the following peculiar manner. Strangling from fluid running down his throat, he would suddenly bring his head forward to expectorate the medicine. Just at this time he would feel a peculiar jumping sensation in his throat and hear a slight click, and immediately thereupon all unpleasant symptoms would disappear.

To this series of cases may be added a case reported by H. S. Wood[7] in 1890, in which the patient, a subject of advanced pulmonary tuberculosis, suffered a dislocation of his hyoid bone. Dr. Wood hurried to the patient's bedside after receiving a message that the patient had displaced a bone in his neck and was choking.

He found the patient, a man of twenty-seven years, sitting up in bed with head thrown slightly forward, arms crossed over the upper part of his chest, one hand grasping the upper portion of his neck as if to steady his hyoid bone, and the other steadying the larynx. He looked emaciated and distressed. There was slight cyanosis. The patient complained of a sensation of impending suffocation and could not at first be persuaded to let go of his neck. After he had done so, Dr. Wood saw the exact state of affairs. There was a certain degree of prominence on the left side of the neck in the region of the submaxillary triangle. On feeling for the hyoid body, it was found to have deviated from the mesial plane of the neck. As he ran his finger along the greater cornu, the tip of the horn was found to be displaced upward and to the left, so as to be on a level with the angle of the inferior maxilla. No crepitus could be detected. While making the patient swallow, Dr. Wood effected reduction by fixing the thyroid cartilage with one hand and pushing the hyoid cornu in the opposite direction to the displacement. Reduction was accompanied by a perceptible click. The dyspnœa improved directly.

At another time a similar dislocation in the same patient, but with less alarming symptoms, was reduced in the same manner. According to the patient's statement the bone was dislocated during a violent paroxysm of coughing with the head bent to the right side.

In this case there was extensive pulmonary and laryngeal disease. Dr. Wood considered that "owing to the degenerative and ulcerative changes in the neighborhood of the hyoid bone and laryngeal cartilages, the ligaments must have been relaxed with general loss of tonicity in the muscles arising and inserted in the hyoid bone."

Excluding the four cases mentioned by Gibb, in which there is no detailed symptomatology, there remain the eleven cases whose histories I have given in brief. While the symptoms vary somewhat in severity, the resemblance between the cases is so striking that the assumption seems warranted that the underlying cause is the same in each case. This is most probably a dislocation of varying grade of the major cornu of the hyoid bone in the direction outward, or inward and downward. Either type may occur as the result of trauma or of sudden movements of the head, neck, or jaws. In the latter case, it seems likely that there exists a loosened condition of the attachment of the tip of the greater cornu of the hyoid bone to the superior horn of the thyroid cartilage and, perhaps, looseness of the articulation of the cornu with the body of the hyoid, allowing freer play of the tip.

The age of the patients varied from seven years to over sixty. In six of the eleven cases, dislocation took place repeatedly. In four, there is mentioned a definite click as the dislocation was reduced. A prominence in the side of the neck between the inferior ramus of the jaw and the sternomastoid muscle was noted in four cases. There was marked dyspnœa in two cases.

In two cases there was local tuberculosis, namely, of the thyro-hyoid articulation and of the larynx itself.

In the cases examined laryngoscopically no change from the normal could be detected.

It is interesting that three of the eleven cases occurred in physicians. Had they occurred in laymen, it is quite possible that they might never have been diagnosed. Most of the milder cases had frequently consulted physicians without a diagnosis being made. The naturally persistent interest the physicians took in their own cases led eventually to the diagnosis.

Subjectively, the patients experienced pain in swallowing (six cases), total inability to swallow (two cases), marked anxiety (four cases), a feeling as though a foreign body were blocking the œsophagus (three cases). In every case there was immediate and marked relief on reduction of the dislocation.

Four cases came on during sudden movements of the neck and jaws (yawning, coughing, singing, etc.), four as the result of direct trauma from without by choking, or from within through the ingestion of a large solid particle.

There is a surprising similarity in the methods of reduction used successfully in each case.

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NOTES ON NEW BOOKS.

For and Against Experiments on Animals. Evidence Before the Royal Commission on Vivisection. By Stephen Paget, F. R. C. S. $1.50. (*New York: Paul B. Hoeber, 1912.*)

Dr. Paget, who has labored so strenuously in defense of animal experimentation, and who deserves unstinted praise for his work in this line, has prepared here, as he states in the preface, "a clear account of the chief results obtained, during the past thirty years, by the help of experiments on animals." This covers discoveries in physiology, in medicine, in surgery, in the use and effect of drugs in tropical diseases, and in diseases of animals and veterinary surgery. All the progress made is stated by the workers themselves in the evidence given by them before

the Royal Commission on Vivisection. In addition to their statements the case of the antivivisectionists is also presented in the same way—their testimony before the Commission being reported with equal detail. For the work Lord Cromer, President of the Research Defense Society, has written a brief but cogent introduction in defense of experiments on animals and the book as a whole is a most important contribution to the literature on the subect and cannot fail to convince all open-minded readers of its fairness and justice. The cause for experiments on animals should be strengthened the world over by this presentation of the case. Those anxious to inform themselves about this question can find no fairer and more temperate exposition of the *pros* and *cons*. There are many unfortunately who cannot be convinced of the justice of experiments on animals, and nothing can be done to bring these people to see light, but others, who may still be in darkness as to the morality of such procedures, will be illuminated by reading this book which is convincing to any fair-minded individual that it is morally right to use animals for research and the solution of problems dealing with health.

Pharmacology. Action and Uses of Drugs. By Maurice Vejux Tyrode, M. D. Second Edition. $1.50. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This work is not intended for the specialist but for students and general practitioners, and both these classes have found it useful. After a brief introduction on "Definitions and General Remarks on the Action of Drugs," the author describes, (1) those "Drugs Whose Constitutional Action is in Greater Prominence"; (2) Ferments, Secretions and Extracts of Animal Organs; (3) "Drugs Whose Local Action is Most in Evidence"; and (4) Drugs of Inorganic Origin. He has accomplished satisfactorily what he undertook to do, and that is to write a pharmacology which should be sufficient for the average man. The publishers have produced a neat book of about 300 pages, but the types used are large and the size of the volume is agreeable.

Pellagra: History, Distribution, Diagnosis, Prognosis, Treatment, Etiology. By Stewart R. Roberts, M. D. Illustrated. $2.50. (*St. Louis: C. V. Mosby Company*, 1912.)

Every new and wide-spread disease calls forth many volumes describing it in various ways, and the literature of pellagra is rapidly growing. Dr. Roberts is an ardent student of this malady, but his gift for writing is not so marked as his industry, and this work shows defects which detract from its value, but many a student and practicing physician will be benefited by reading it, since it covers the ground thoroughly. The style of the author is too fine and aphoristic, and needs tempering. The following sentence is typical; speaking of pellagra the author says, "It is a disease of many symptoms and of many variations; its only consistency is its inconsistency; it seems cured and yet recurs; the pellagrin seems to be approaching his end and yet lives for many years; it spreads and is not contagious; the offspring of the pellagrin receives his mark and yet it is not inheritable; it is not and appears; it is and disappears; it is a morbid entity and yet it contains within itself many lesser morbid entities; it falls with equal right in the sphere of dermatology, neurology and gastrology, and yet it is a general disease; divers diseases become one, and this one is pellagra; there is no pellagra—only the pellagrous." There are certain terms used by the author which are ill-chosen as, for example, "convalescent pellagra," the word convalescent is certainly more correctly applied to the patient than the disease. Again and again he speaks of the neurasthenia or neurasthenic symptoms of the pellagrin. So much obloquy is usually attached to neurasthenia that it seems unkind to the pellagrin to accuse him of showing this, and besides leads to confusion. Dr. Roberts employs the words "dermotagra" and "dermotagrous," which really are the exact equivalents of pellagra and pellagrous, and would apply them simply to the condition of the skin, but this too is unnecessary and confusing, and to have "pellagrous dermotagra" seems redundant to say the least. These are minor defects and we do not mean to lay too much stress upon them. Numerous bibles are famous for misprints and this work is likely to become a classic from one faulty translation. "*Maladie de Saintes Mains* —the sickness of the main saints."

Les Origines de la Trépanation Décompressive. Trépanation néolithique, trépanation pré-Colombienne, trépanation des Kabyles, trépanation traditionelle. Par Le Dr. Lucas Champonnière, etc. (*Paris: G. Steinheil, 1912.*)

As the introductory chapter of a large work on trepanning, the author has published this most interesting historical essay separately. Three Frenchmen, Premières, de Baye and Broca, had published earlier works on this subject and in this country Muniz and MacGee wrote a notable book on "Primitive Trephining in Peru" in 1897. But Dr. Champonnière, a brilliant surgeon, who has performed many decompressions and written much on this subject, has made a more thorough study of the question than any of his predecessors, and his monograph, with thirty-two illustrations, is the most authoritative work we have. There are certain features connected with the prehistoric skulls, which were trepanned, for which there is no explanation. What were the symptoms which led to the operation? none of the trepanned skulls show any signs of fracture, so it is questionable whether the operation was done to relieve the effects of such injuries. Why were the buttons of bone preserved? for some of these have been found. Trepanning is an interesting phase in the life of prehistoric man about which we can speculate at length, and which is likely never to be satisfactorily explained, but many will find Dr. Champonnière's essay both entertaining and instructive.

From the publishers William Green & Sons (Edinburgh and London, 1912) we have received a brief pamphlet entitled, The Local Incidence of Cancer. (Price 1/.) Its author Charles E. Green, F. R. S. E., advances the theory that cancer is due to the consumption of coal, but his evidence seems far from convincing.

Surgical After-Treatment. A Manual of the Conduct of Surgical Convalescence. By L. R. G. Crandon, M. D., and Albert Ehrenfried, M. D. Second Edition. Thoroughly Revised. Illustrated. $6. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

This is an excellent and most useful book and its second edition so soon after the first is most gratifying. For the student and practitioner, who has had but slight hospital experience, the work is invaluable. It is well written and the advice given is sound and practical. The illustrations are well chosen, but it is a pity that many of them are rather hazy, not as sharp-cut as they should be to adorn this otherwise first-rate production.

The Collected Works of Christian Fenger, M.D. Illustrated. Two volumes. $15. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

The friends of Dr. Fenger, as a memorial to him, have had all his papers, with a few exceptions, reprinted in handsome form. Fenger was for many years the leading pathologist and one of the leading surgeons in Chicago, and this tribute is no more than his due. He was one of the brilliant group of physicians in Chicago during the last quarter of the past century and did

much to elevate the standards and ideals of the profession there. His ability was marked, and this collection of papers shows the breadth of his knowledge and interest in his work. He was no surgical specialist, but had trained himself to be a fine general surgeon and his writings cover a broad field, and demonstrate as well the successful qualities of his work, as the fine character of the man.

A Collection of Papers, Published Previous to 1909. By William J. Mayo and Charles H. Mayo. $10. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

It is now possible for him who wants it to secure practically all that has been written by these two famous brothers. With the addition of these new volumes to those that have recently appeared from the staff of St. Mary's Hospital the writings of the Mayos can be had in book form. How much these volumes will add to their fame is problematical. To-day their clinic is a kind of Mecca, visited by surgeons from all over the world, not only to witness operations by these brilliant men, but also to see how they have organized the best private surgical clinic in the world.

But there will be readers who will enjoy studying these volumes to note the evolution of the ideas and practices of the Mayos and from this point of view the volumes will be most instructive and valuable. They are splendid evidence of the constant activity, thoughtfulness and broad interest of these most remarkable men, who in their joint-work, remind one somewhat of the Wright brothers, devoted to each other, and working with the highest of principles.

Collected Papers by the Staff of St. Mary's Hospital. Mayo Clinic, Rochester, Minnesota, 1911. $5.50. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

In this volume are all of the papers read or published by any member of the staff of the hospital during the year 1911. Some of these have already appeared in the medical journals, others will appear later. There are twenty-three contributors with nineteen papers on the alimentary canal, one on hernia, sixteen on genito-urinary questions, four on ductless glands, three on the thorax and its extremities, three on technic, and seven general papers. The volume has a good index, and some of the papers are well illustrated. The staff of the Mayo Clinic has now become so large that, although much more work is being turned out now than earlier, it is losing the very distinctive and interesting character it had when the Mayo brothers were to all intents and purposes the staff. They have now associated many workers with them and as a necessary result the work produced is uneven, and lacks the mark of genius exhibited by the founders of this extraordinary clinic.

An Essay on Hasheesh. Including Observations and Experiments. By Victor Robinson, Pharmaceutical Chemist, Columbia University. 50 cts. (*New York: Medical Review of Reviews, 1912.*)

After experimenting on himself and some of his friends with this drug, the author has written a brief essay relating his own experiences as well as those of his friends. He introduces his essay with a brief account of the drug in history and medicine. Mr. Robinson has not hesitated to give the names of those he experimented upon, which, as all he tells of them is not pleasant, indicates a certain lack of delicacy on his part, and leaves a disagreeable and unsatisfactory impression of his work, which is doubtless intended seriously, but seems lacking in true scientific spirit. The essay is brief and is unimportant as adding anything new to our knowledge of hasheesh and its effects.

What To Do in Cases of Poisoning. By William Murrell, M. D., F. R. C. P., etc. Eleventh Edition. $1. (*New York: Paul B. Hoeber, 1912.*)

This guide has been popular for many years in England, and may well become so in this country, but in another edition should be carefully revised, so as to eliminate some poisons (plants and quack remedies) used abroad that are unknown here, and others met with here inserted in their place. It is a very small volume that a practitioner who carries a bag can always have at hand to use in an obscure case, and the advice contained is good. All the poisons are arranged alphabetically so it is easy to look up their symptoms and antidotes.

The Care of the Skin in Health. By W. Allan Jamieson, M. D., F. R. C. P. (Eng.). $1. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

This is a very brief essay intended for the laity, and as such can be recommended with safety, for it is simply and clearly written and none could go astray in following the author's advice. The only objection to it is its cost, for it could be widely distributed with benefit among the intelligent poor if only its expense were reduced, as could easily have been done.

Sexual Impotence. By Victor G. Vecki, M. D. Fourth Edition. Enlarged. $2.25. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

For the general practitioner this book may serve its purpose, but for the profounder student of the subject it lacks real scientific value. Its importance was not so great as to make it worthwhile to reprint the book.

Franklin's Contribution to Medicine. By Theodore Diller. $2. (*Brooklyn, New York: Albert T. Huntington, 1912.*)

In a neatly printed volume Dr. Diller has collected the writings of Franklin which deal with medical questions; almost all he wrote on the subject is to be found in letters addressed to many correspondents, and here, for the first time in English, Franklin's views on this science have been brought together. This makes the essay an important contribution to medical history. That Franklin took a lively interest in medicine is not strange, for he had a mind of exceptional breadth, and always had a desire to be well informed on all scientific questions and associated himself with the most intelligent men in America and Europe. Philadelphians, especially, but all Americans owe him a debt of gratitude for his efforts in founding the first medical school in America; that it was born is largely due to him. Franklin's views on hygiene were exceptionally sound for his time, and all physicians will be glad to acquaint themselves with his ideas on this branch as well as others related to medicine.

Children: Their Care and Management. By E. M. Brockbank, M. D. (Vict.), F. R. C. P. $1.50. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

There are numberless books on this subject, but the numbers of young mothers and nurses is constantly growing, so that there are always readers for a new book of this kind; and many a young doctor will find it useful also. It deals with infants and children up to the age of eight or ten; and takes up all the essential points that should be carefully considered in their upbringing, such as nursing, washing, clothes, diet, environment, etc. In no way does it lead mothers or nurses to intrude upon the proper province of the doctor, in which respect many of the books on this subject err, and while the advice given on many

points seems rather cursory, it is sufficient for all intents and purposes. The book contains good counsel and compares favorably with the majority of similar works.

The Surgical Clinics of John B. Murphy, M.D. June, 1912, Vol. I, Nos. 3 & 4. $8 per year. Bi-monthly. (*Philadelphia and London: W. B. Saunders Company.*)

There is a vividness about these Clinics which portrays well the nature of Dr. Murphy, and the excellent quality of his work. The method of presentation will doubtless add to the popularity of these talks at the operating table. Many different surgical questions are discussed in these numbers, and if read with care a student will get valuable hints from them.

Studies in Cancer and Allied Subjects: Pathology. Conducted Under the George Crocker Special Research Fund at Columbia University. Vol. II. (*New York: The Columbia University Press, 1912.*)

This volume opens with a brief but adequate introduction by Dr. MacCallum, who sets forth clearly the difficulties inherent to the solution of the cause of cancer. This is followed by a series of twenty-seven papers by Levin, Siltenfield, Lambert, Hanes, Frank, and Unger. Some are the combined work of Levin and Siltenfield, Lambert and Hanes, and Frank and Unger, but a majority are written by Levin and Lambert alone. All these papers have appeared elsewhere, but as the product of work done with the aid of this fund it is well to have them collected in this form. Some of them are little more than very brief preliminary notes, of only a page or less in length. There are a number of beautiful illustrations, and as a piece of press work the volume deserves commendation, though we question the need and, if not needful, the righteousness of publishing so costly a volume at the expense of the fund. Several other volumes dealing with the cancer problem are in preparation, and there is no doubt that the series will form a most important contribution in the elucidation of the problem. The work done already by the men mentioned augurs well for what is to follow, and the report is one which all students of this and allied problems must have at hand.

The Mechanistic Conception of Life: Biological Essays. By Jacques Loeb, M. D., etc. $1.50. (*Chicago, Illinois: The University of Chicago Press, 1912.*)

The author, known to scientists as a most brilliant and original worker along certain lines, has unfortunately to the public, if it knows him at all, a sensational newspaper notoriety because of some of his early investigations into artificial parthenogenesis. It is to be hoped, however, that these essays may make him better known to serious readers that they may learn what a profound thinker and extraordinary investigator Jacques Loeb is. These cannot be called "popular" essays, but with little trouble their essential meaning can be grasped by careful reading, and they cannot fail to stimulate the student's interest. They have already appeared elsewhere in various publications, so that there is necessarily some repetition of facts in this volume, but some of the problems discussed by the author are better for this repetition, as they are not at first reading always easy to comprehend. This volume may be called "entrancing"; and all eager to know more of the origin of life will find no modern book of its size nearly so instructive, or inspiring.

Practical Anatomy. By John C. Heisler, M. D. $4.50. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

Bound in flexible covers this anatomy is certainly practical for a laboratory worker, but why should the term "practical anatomy" be used any longer, since all anatomy is practical if applied to a definite end? Dr. Heisler's book is sufficiently illustrated and well printed, but the reason he gives in his preface for not using the more advanced nomenclature [B. N. A.] does not seem to us to carry much weight. If those, like himself, who believe in it will not use it, then it will never become universally adopted; why it will be easier to adopt the nomenclature later rather than now is not evident. Points of special clinical interest concerning structures under discussion are introduced in smaller type. This is done to hold the interest of the student. It does not seem that this is a very wise procedure; such points are multifold, and no two authors would agree as to which had better be inserted or omitted. The result is a product like the majority of illustrated medical dictionaries; the illustrations are chosen quite hap-hazard, and add little or no value to the work. The author takes up in sequence the upper limb, the lower limb, the head and neck, and the abdomen and thorax, and for the student who wishes to get through his anatomy without the labor required to master Gray's classic, this anatomy will serve well.

Oxford Medical Publications: Gonococcal Infections. By Major C. E. Pollock and Major L. W. Harrison. $2. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

The authors, both of whom belong to the Royal Army Medical Corps, have written a small and simple book, which is, however, hardly sufficient for even the general practitioner. After discussing the pathology of the gonococcal infections, they consider both vaccine and serum therapy for these, and then describe the infections in men, women, and children and the proper treatment for each. The work concludes with a very brief chapter on gonococcal septicæmia. Only a superficial knowledge of the troubles which are due to an infection with the gonococcus can be derived from a reading of this publication.

Die physikalische Therapie der Gelenkkrankheiten für Aerzte und Studirende. Von Dr. Eduard Weisz. $1.50. (*Berlin and Wien: Urban & Schwarzenberg; New York: Rebman Company, 1912.*)

This treatise on the treatment of diseases of the joints is divided into two parts—a general and a special. In the first the author takes up all the various physical methods and describes their proper employment, while in the special part he discusses more fully their practical application to congenital joint troubles, neoplasms, joint neuroses and traumas, bacterial joint infections, and diseases of the joints due to metabolic disturbances. It is a serviceable work to any student who reads German easily, although it deals but slightly with operative procedures, but the value of rest, extension, light, electricity, hyperæmia and many other measures is well shown. It is a useful small manual for the general practitioner rather than the specialist.

A System of Treatment. In Four Volumes. Edited by Arthur Latham and T. Crisp English. (*New York: The Macmillan Company, 1912.*)

There has been almost an epidemic of publication of exhaustive treatises on therapeutics, and several large works have come out in the last year or two. The writers of this one are on the staff of St. George's Hospital, London, an institution from which much excellent work has come. This system has two peculiarities which arrest the attention at once; the four volumes appear simultaneously and each volume has a complete index to the whole work. Another point worthy of mention is the success of the bookmaker's art. Each of these volumes contains over four-

teen hundred pages and yet they are of convenient size and weight. It does seem as if American publishers might learn a little in this regard from their brethren abroad and give us books which are less cumbersome to handle.

It is impossible for one reviewer to discuss such a work in detail, particularly as it includes medicine, surgery, tropical diseases, dermatology, diseases of the eye, obstetrics and gynecology, not to speak of other subjects. The general impression is that the work as a whole is most satisfactory. The discussion of treatment is usually complete and according to the best modern standards. The editors have made the effort to include the most recent advances which are worthy of notice. There are many general articles which add to the value of the work, as for example on the management of the sick room, surgical technique, shock, poisons and antidotes, etc. Treatment by vaccines receives a considerable amount of attention. It may be said that one can find information on practically any question concerned with therapy.

The editors comment on the difficulty of arrangement and they have doubtless solved their troubles in the best way possible. However, it is difficult to see why acute abscess and whitlow are put under infective diseases. Again, why should tuberculosis be divided and discussed here and there? Why is acute tuberculosis under the infective diseases and pulmonary tuberculosis under diseases of the lungs with tuberculous meningitis in a separate section? Would it not have been better to bring together the whole discussion of tuberculosis in one section? The same comment applies to syphilis. Certain infections are considered quite apart under the heading of Tropical Fevers; malaria, Malta fever and plague are among these. Under the heading of Abdominal Tropical Diseases we have cholera and dysentery among others. These diseases are by no means confined to the tropics and this seems an artificial arrangement. However, it must be said that the complete index in each volume renders it easy to find the reference to a particular disease. Those who have struggled with the difficulties of classification will be ready to sympathise with the editors in the attempt to do the best with this question.

As is natural the articles vary greatly in fullness and value, for the editors of such a work have great difficulty in securing even a degree of uniformity. Take for example the section on nephritis. The discussion of the medical treatment of chronic interstitial nephritis occupies a little more than a page, while the surgical treatment of nephritis occupies nearly double the space. Surely this is not a proper disposal of space. It is a pleasure to turn to the discussion of appendicitis, for the article is a splendid one by the surgical editor (Mr. English), and in it the attitude towards early operation is to be highly commended. Attention is drawn to this as the writer has recently gone over this question in some English and German works in which the opinions expressed deserved strong condemnation. It is to be hoped that this section will be widely read, digested, and acted upon in practice.

It is not to be expected that any reviewer would agree with every part of such a work and if he is looking for opinions to disagree with there is no difficulty in finding them. However, there are some points which are deserving of mention. Under typhoid fever, constipation is given as a sign that milk is not agreeing. It would be interesting to know the reasons for this; most of us would take exactly a contrary view. The view that carbohydrates should be withheld is also against the general opinion. The use of the tub bath is discussed as an antipyretic measure. This mistaken idea dies hard and it is a pity that the editors did not correct it. We meet an old friend, the Woodbridge treatment, and one hardly knows whether to laugh or weep. The editors certainly nodded here. We fail to find any mention of the use of hexamethylenamin in typhoid fever, which is a serious omission. The article on diabetes mellitus is a very satisfactory one, especially in its clear and specific directions. James Mackenzie contributes an excellent discussion on the treatment of cardiac conditions with an especially clear exposition of the general principles of therapy in this domain. A suggestion which may be made is that a fuller discussion of the value of strophanthin given intramuscularly would be an advantage. This is one of the greatest additions to cardiac therapy of recent years.

The first and second volumes discuss general medical and surgical treatment. Surgical measures are fully taken up and the articles are well illustrated. As a matter of interest the subject of mucous colitis was selected for comment. Some space is given to the surgical treatment and it is interesting to find what the writer considers mucous colitis to be. He apparently limits the term to cases in which there is an inflammatory condition present. As the term is generally used in this country such a finding would exclude the diagnosis of mucous colitis. As the author does not believe in a mucous colitis secondary to a general nervous condition, it is evident that his views have to be carefully understood before his article has any value to the reader. In the discussion of the treatment of diseases of the nervous system, the editors have been fortunate in securing a brilliant list of contributors and these sections are excellent throughout. One name is persistently misspelled, that of the man who described the re-education exercises so useful in tabes; this appears as Fraenkel instead of Frenkel.

The third volume deals with special subjects; many therapeutic methods, including vaccine and serum therapy, are discussed, and tropical diseases, those of the eye, nose, throat, and skin diseases are included. The fourth volume deals with obstetrics and gynecology.

This system should prove especially useful for the general practitioner as he can find information on any subject. The full index adds greatly to its value. Altogether we can cordially recommend it and congratulate the editors on their success.

Diagnose der Simulation nervöser Symptome. Ein Lehrbuch für den Praktiker. Von Priv.-Doz. Dr. Siegmund Erben, Wein. $2.15. (*Berlin and Wien: Urban & Schwarzenberg; New York: Rebman Company, 1912.*)

This is a valuable work on the differential diagnosis of organic nervous troubles and simulated nervous symptoms. To decide whether a symptom is really of organic origin, or purely functional is oftentimes one of the most difficult tasks that the physician can perform—an exact determination cannot frequently be arrived at. It is often said "time alone can tell," but this is not absolutely true, for though a symptom apparently functional in nature may disappear after a longer or shorter interval, there is no final proof that it was not due to some real organic lesion. In fact the more we learn of disturbances of the human system, the less becomes the number of conditions which can rightly be classified as functional. In medico-legal cases arising from accidents the question of the simulation of the symptoms is frequently the cause of much divergence of opinion among experts, and this careful study of Dr. Erben's will help the general practitioner from falling into avoidable errors. He begins with a study of nervousness, neurasthenia, and the neuroses of accidents and their various forms of expression in different organs, and in a similar way discusses anæsthesia, hypæsthesia, paræsthesia, pain, hyperæsthesia, motor symptoms, dizziness, sensation of illness, attacks of unconsciousness, epilepsy, hysteria, coma, and insanity. The monograph forms an important addition to the study of nervous diseases, and also to psychiatry, for after all if a symptom is simulated it is above all essential that the mental condition of the patient should be studied.

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THE BENCE-JONES PROTEINURIA IN CONDITIONS OTHER THAN MYELOMATOSIS: AN INSTANCE ASSOCIATED WITH METASTATIC CARCINOMA.*

By T. R. Boggs, M. D., and C. G. Guthrie, M. D.

(From the Clinical Laboratory of The Johns Hopkins University and Hospital.)

Since Kahler[1] first pointed out the association of Bence-Jones proteinuria with multiple myeloma, his observations have been substantiated by numerous reports. This relation holds in the great majority of instances of the disease, but is not constant. Not all cases of myelomatosis exhibit this peculiar body in the urine, for, disregarding such as were recognized only at autopsy and all in which the urine was insufficiently studied during life, there remains a considerable number of careful observations in which no trace of this protein was found after repeated and long continued search, (Parkes Weber[2]; v. Jaksch,[3] 3 cases—one over a period of 2½ to 3 years; Scheele and Herxheimer[4]; Collins[5]).

The intermittent excretion of Bence-Jones protein in this disease has been commented upon by a number of authors, while Kühne,[6] Conti,[7] and Anders and Boston[8] have reported cases in which the peculiar body disappeared from the urine some weeks or months before death.

Again, the Bence-Jones protein has been found in conditions other than multiple myeloma. Such cases are rare and require close scrutiny as not a few of the reported instances are open to doubt with regard to the accuracy of the determination of the protein or the correct interpretation of the pathological findings. Until recently, the Bence-Jones body, now known to be a true protein, was described as an albumose and much confusion has arisen from the fact that traces of albumose have been found in many febrile and cachectic conditions. Some observers through insufficient attention to the reactions differentiating albumose from Bence-Jones protein have failed to distinguish them correctly. In the cases from the literature appended below, special mention will be made of any in which the urinary findings were insufficiently detailed to assure the identification of the Bence-Jones body. From the pathological standpoint there has also been confusion regarding the nature of the bony changes. Taking into consideration these two sources of error, chemical and pathological, we have collected from the literature such cases as seemed to be clearly defined from both standpoints.

The earlier cases of multiple myeloma associated with this unusual body in the urine were described as osteo-malacia (Bence-Jones, Macintire and Dalrymple[9]; Stokvis and Kühne[l.c.]). Jochmann and Schumm[10] originally reported a case of Bence-Jones proteinuria with autopsy as osteomalacia but after Bradshaw's[11] criticism, it was republished as one of multiple myeloma. Raschkes,[12] however, has described an instance of Bence-Jones proteinuria, in which apparently the post mortem examination revealed a true senile osteomalacia. Seegelken's[13] case of chondrosarcoma would probably now be classed as multiple myeloma. Campbell-Horsfall[14] observed a transient excretion of the Bence-Jones body lasting a few days, as a result of a gunshot wound in the leg. Fitz[15]

* Read at a meeting of the Philadelphia County Medical Society, October 23, 1912.

detected this body in the urine of a patient with myxœdema in whom no bone changes were observed, but as no post mortem examination was made, the possibility of some involvement of the marrow cannot be excluded. References to a similar case reported by v. Jaksch[16] seem to be erroneous as the original article mentions only a nephritic albuminuria. We have found in the literature three undoubted cases in association with lymphatic leukæmia (Askanazy[17]; Decastello,[18] 2 cases). In this class also belongs the case which Weinberger[19] reported as chloroma, if we accept his unsupported statement that the Bence-Jones body was present.

Again, this protein has been found associated with metastatic involvement of the bones from a primary tumor situated elsewhere. Oerum[20] described such a finding in a patient with carcinoma of the stomach and multiple metastases to the bones. The patient was 39, a laborer, who had suffered for six months with diarrhœa; later he developed pains in the bones of the shoulder, pelvis and legs; paræsthesias and flimmer scotoma; loss of weight; and symptoms of gastric stenosis. In the urine Bence-Jones protein was found in small quantities, 0.25-0.5 gm. per litre on several examinations, but gradually diminishing in amount before death, which occurred seven months after the onset of symptoms. No other protein was present. The autopsy showed typical metastases from the gastric carcinoma, widely disseminated in the bones. So far as we have been able to ascertain, this is the only well established instance of the kind hitherto recorded.

Others have reported cases possibly referable to metastatic foci in the bones, but not substantiated by autopsy; Boston,[21] in a woman, who developed a characteristic proteinuria with bone symptoms, four years after the removal of a cancer of the breast; Martin,[22] in a woman before and after operation for ovarian neoplasm; Hirschfeld[23] in a man with abdominal tumor. The two latter authors make the statement that the Bence-Jones body was found but give no details as to the methods employed for its detection.

The foregoing cases, with our own which follows, have an important bearing upon the theoretical consideration of the relation of Bence-Jones proteinuria to multiple myeloma.

Case History *: E. B., white female, 37. Admitted to The Johns Hopkins Hospital April 22, 1912. Died May 9, 1912.

Complaint.—Rheumatism.

Family History.—Father supposed to have died of cancer.

Past History.—Unimportant.

Present Illness.—Began six months before admission with onset of sudden pain in the right hip, which increased so that she was obliged to stop work two weeks later; great difficulty in walking. After two months, a similar trouble appeared in the left hip. Coincident with the joint trouble, she noticed increasing nervousness, numbness of the hands and awkwardness. Appetite poor. Occasional vomiting unassociated with pain. Loss of 40 pounds in weight. Four weeks ago she noticed a painful lump in the right breast. The discovery of this lump was not elicited in taking the history but during a physical examination.

Physical Examination.—Patient much emaciated. Slight general pigmentation, most marked in folds of the skin. *Lungs* clear. *Heart* normal. Hard, irregular mass in right *breast* with retraction of the nipple and some puckering of the skin. *Abdomen* normal. *Reflexes* normal. No local or general *glandular* enlargement. *Bones:* Spine somewhat stiff. Some shortening of right leg. Tender node on sixth rib—right side—below breast. *Blood pressure:* 140 mm. Hg. *Blood:* Red blood cells: 4,000,000; white blood cells: 9,200; Hb. 74%. Differential count: normal. Wassermann: negative.

An extensive *radiographic* study by Dr. Baetjer was reported as follows: "X-ray examination shows carcinomatous metastases in skull, ribs, both trochanters, both ilia, and right tibia. These foci are slightly different from ordinary metastases in that the areas involved in the bones are sharply limited and do not seem to be invasive in character. The metastatic areas in the bone at first glance present an appearance, somewhat like giant cell sarcoma, as there is definite new bone formation around the edge, as though an attempt had been made to limit the disease."

Urine.—Acid, clear, 1012 to 1018. No sugar. No casts. No red or white blood cells. Occult blood test (guaiac)—negative. Layer test with HNO_3 gave an immediate well defined white ring at the point of contact. With cold acetic acid there was no precipitate. With heat and acetic acid, there was a precipitate at 60° C.—partial clearing on boiling—reprecipitation on cooling. The filtrate from this reaction gave no test for protein (Biuret). The washed precipitate obtained by heating to 60° C. was soluble in warm dilute Na_2CO_3 and remained in solution after dialysis; then giving the characteristic reactions for Bence-Jones protein in the pure state. On the addition of one drop of 25% HNO_3 to a few cubic centimeters of the urine in a test tube there was an initial turbidity which cleared up on shaking. The addition of a few more drops of acid caused a precipitate in the cold—almost completely soluble on boiling—and reprecipitated on cooling. With two volumes of saturated ammonium sulphate solution there was complete precipitation—with resolution on dialysis. Total amounts of urine were studied for nine days—up to 48 hours before death. Incontinence for last two days—no urine collected. In this study it appeared that on days 1 to 4 inclusive, and on the 7th day, Bence-Jones protein alone was present in the urine, while on the 5th and 6th days, traces of serum albumin were discovered in addition to the Bence-Jones protein. On the 8th day Bence-Jones reaction was doubtful and serum albumin was present, while on the 9th day, no Bence-Jones body was detected but serum albumin was found. On these two days the urine was strongly alkaline and somewhat putrid. The total protein varied between 0.25 and 1.25 gms. per litre (Tsuchiya). From the combined urines of five days the Bence-Jones protein was isolated by precipitation with two volumes of saturated ammonium sulphate solution and dialysed until chlorine-free, the process being repeated three or four times, when a clear neutral, slightly amber colored fluid was obtained which gave all the characteristic reactions for Bence-Jones protein in the pure state. Owing to the accidental loss of our material we were unable to complete an elementary analysis.

During the short period of observation, spontaneous precipitation of the protein did not occur.

Careful renal functional tests were made by Drs. Fitz and Rowntree. These showed a phenolsulphonephthalein excretion of 23% for two hours: lactose 8%; iodide present after 72 hours; total chlorides, 0.15-0.18% of the amount ingested.

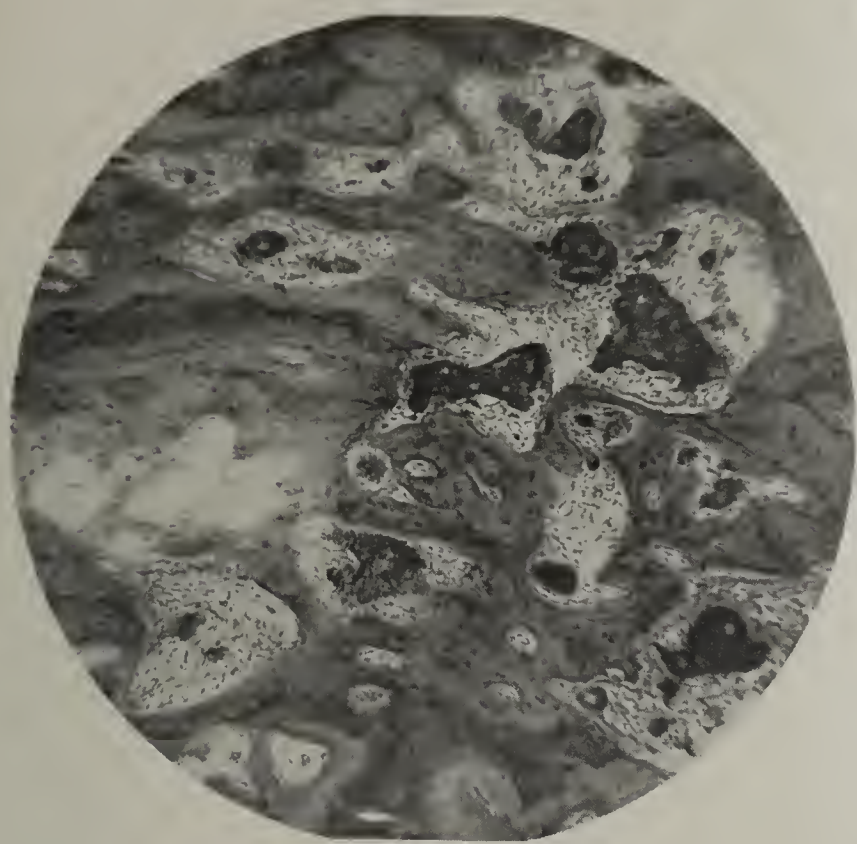
The patient became rapidly weaker and semicomatose, with loss of sphincter control, difficulty in swallowing, and feeble, irregular heart, death occurring on May 9th.

No autopsy was secured, but a portion of the femur was removed for histological examination. For the following report on this we are indebted to Dr. Joseph C. Bloodgood.

Pathological Diagnosis.

Section I. Bone and Tumor.—Epithelial cells of the glandular type in alveoli of different sizes and shapes, surrounded by a

* This case was reported briefly by the authors in a previous communication. Trans. Assoc. Am. Phys., 1912.



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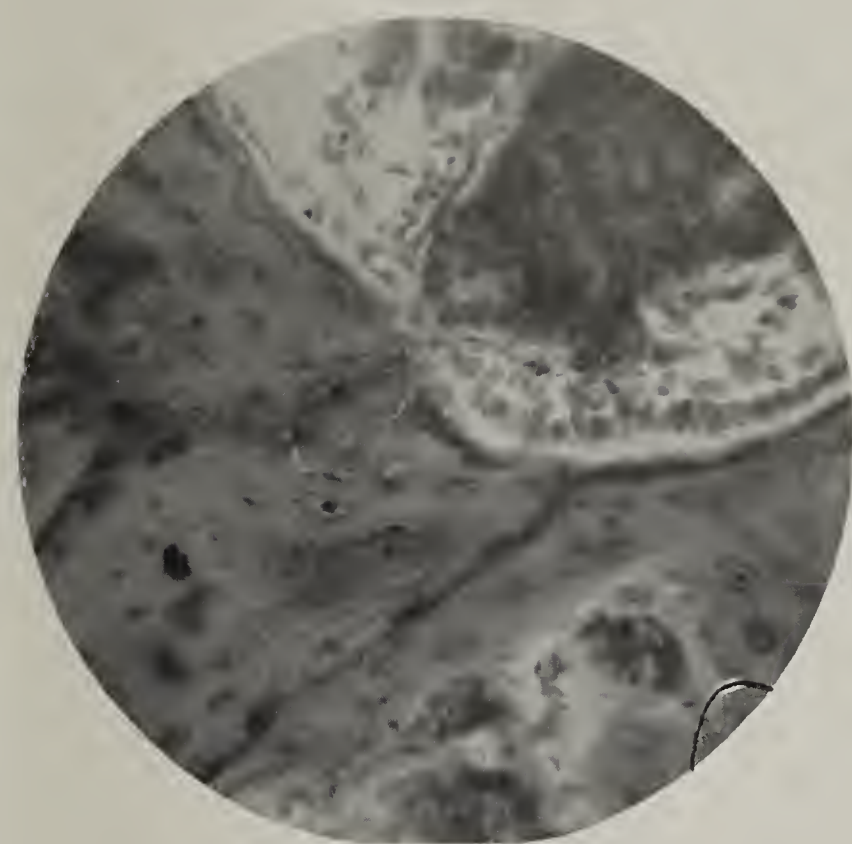

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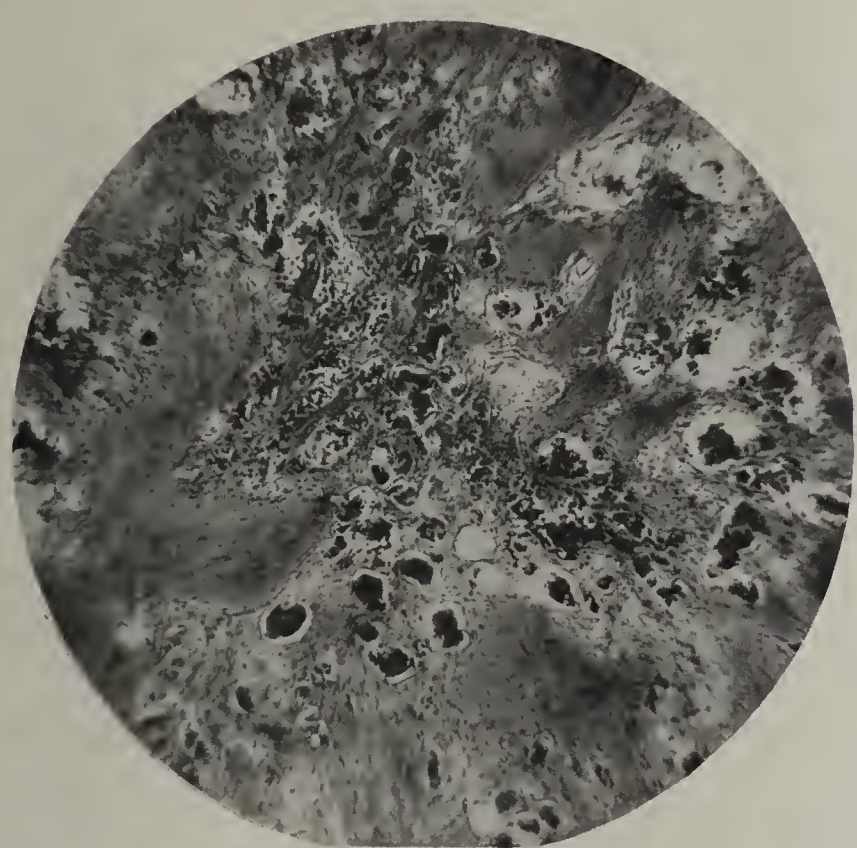

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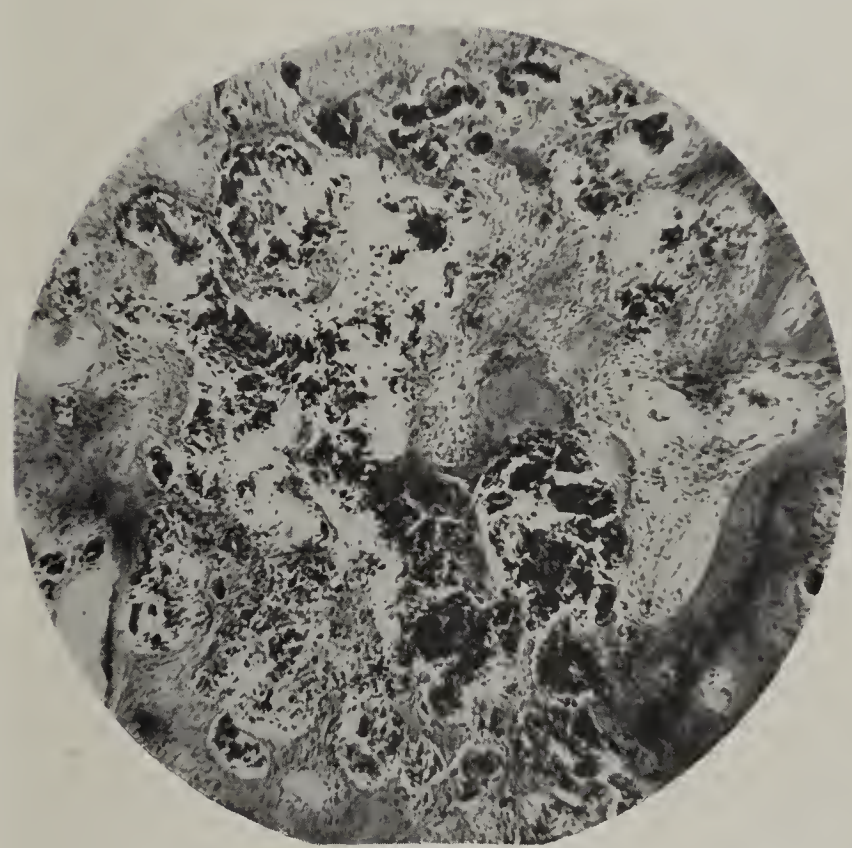
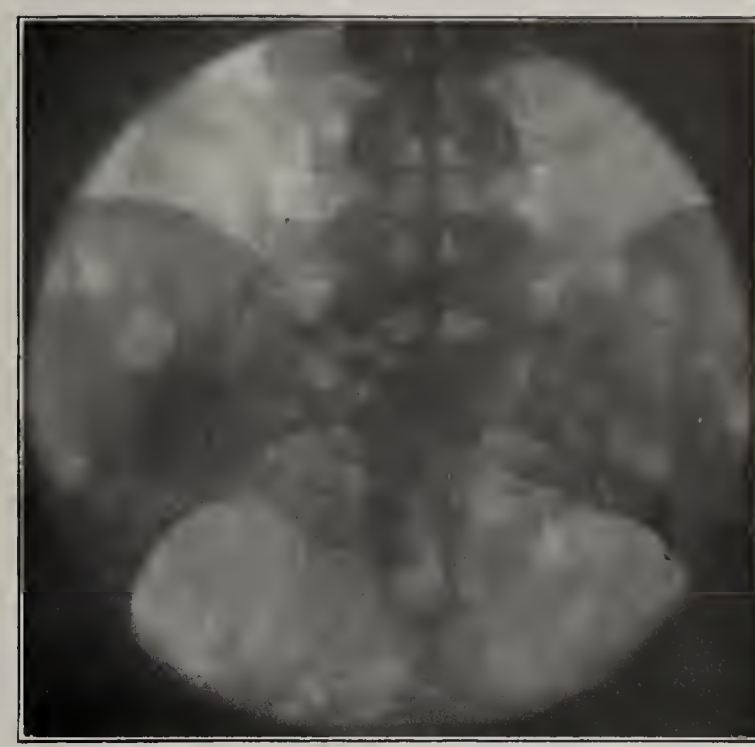


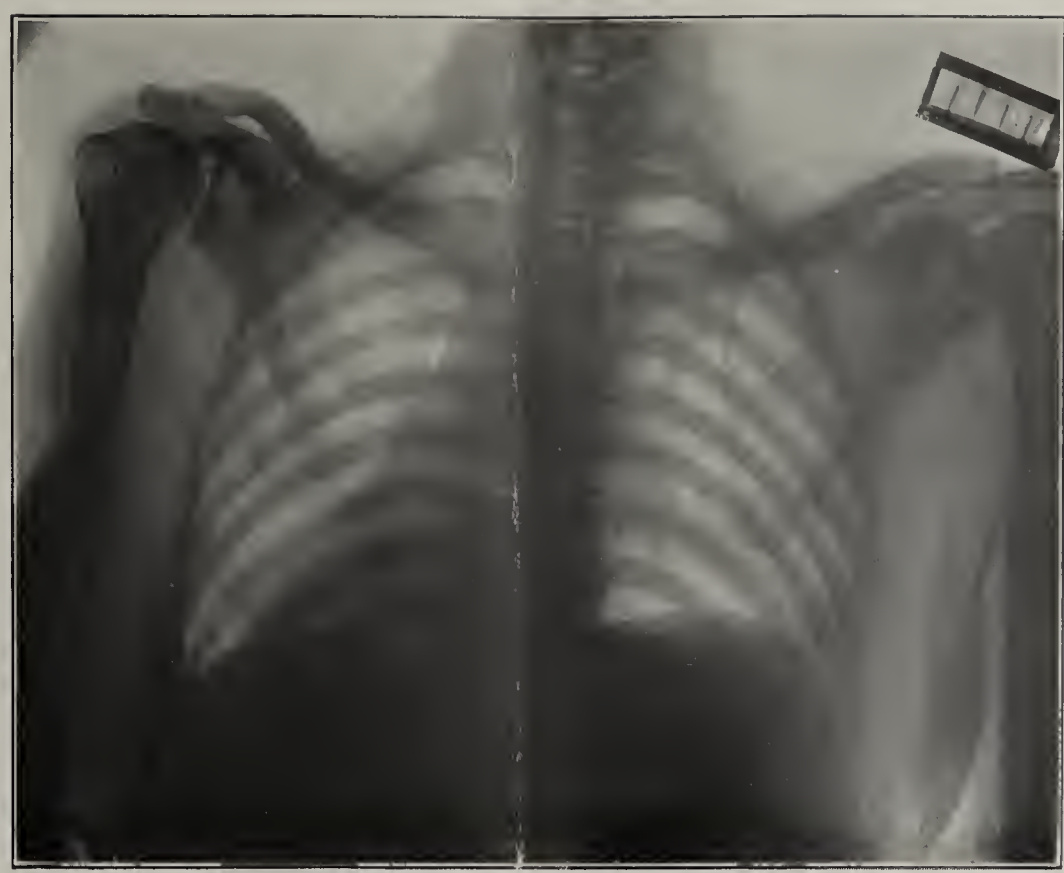
4

TUMOR AND BONE FROM FEMUR.

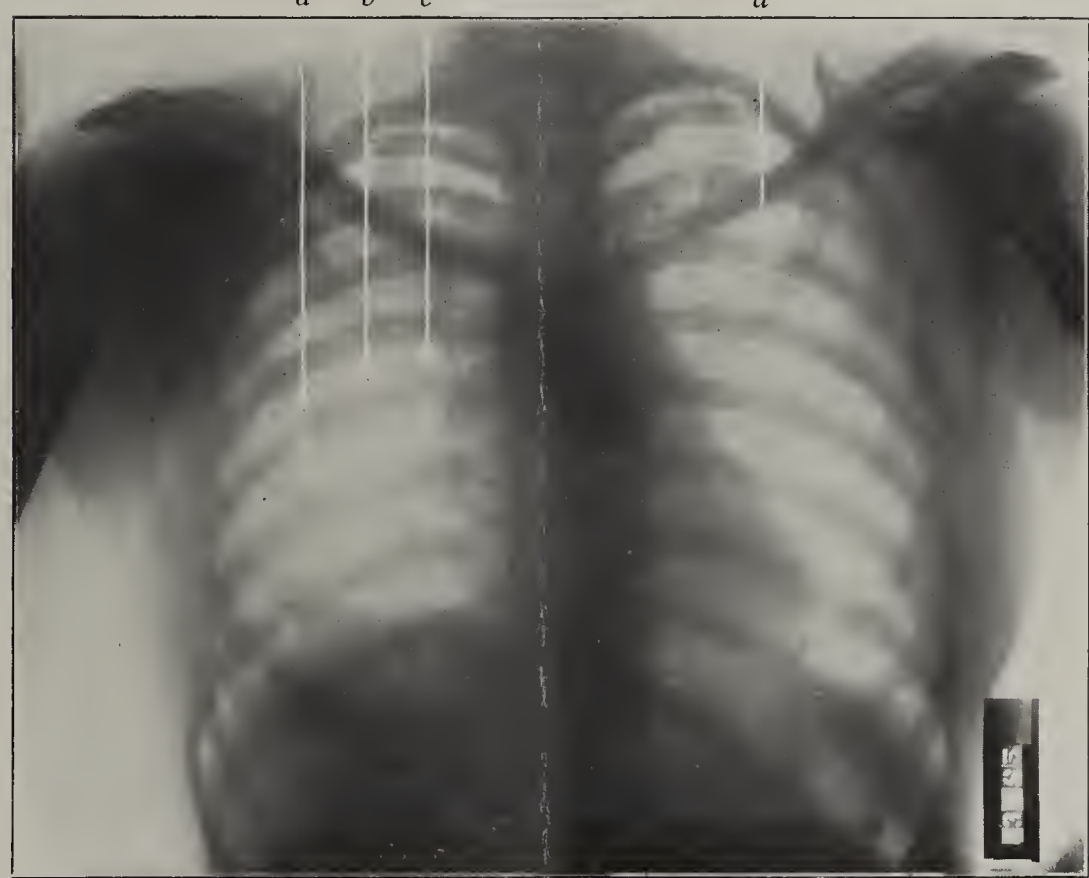
Section I. 1 and 2, low and high magnification.
Section II. 3 and 4, low and high magnification.



Metastatic Nodules in Skull, Pelvis and Long Bones.



Metastatic Nodules in the Ribs.



Anterior View of Thorax.

a, *b*, *c*, *d*, metastatic nodes in the ribs.

rather dense fibrous stroma. In this stroma there are two types of bone areas: old bone showing lacunar absorption by the cancer cells and typical islands of new bone formation of the endosteal cell type. This was first described by von Recklinghausen as osteitis carcinomatosa.

Section II. Bone and Tumor.—Shows in addition, medullary fat tissue, normal cancellous bone, with islands of cartilage formation, cancer infiltrating and absorbing cancellous bone, fewer areas of new bone formation.

In the case here reported there can be no doubt of the nature of the pathological process and the presence of the Bence-Jones body in the urine was clearly demonstrated, making the second authenticated instance of the sort on record.

In collating the foregoing material we are struck by the fact that all the cases of Bence-Jones proteinuria have one point in common—namely, the more or less extensive involvement of the bone marrow, Fitz's case excepted, in which no examination of the bone marrow was made. It is also obvious that the relation of multiple myeloma to Bence-Jones proteinuria cannot be specific, for we see that other disease processes involving the marrow may lead to the excretion of this unusual body. The excretion of the protein seems also to bear no fixed relation to the extent or duration of the disease process, as it may appear in the urine before any demonstrable bone lesions occur (Boggs & Guthrie[26] have reported a case without bone symptoms and with normal skiagrams), and may disappear at a time when the lesions in the marrow are most extensive. Again very wide spread involvement of the bone marrow may occur unassociated with this type of proteinuria. In illustration of this point the following table is appended:

Diverse Bone Involvement Without Bence-Jones Proteinuria.

Cases.	Diagnosis.	No.
Parkes Weber[2]	Multiple myeloma	1
v. Jaksch[3]	Multiple myeloma	3
Scheele & Herxheimer[4].	Multiple myeloma	1
Collins[5]	Multiple myeloma	1
Stokvis—cited by Kühne[6].	Multiple osteosarcoma	1
Markwald[24]	Intravascular endothelioma, practically all bones of body involved.	1
Naunyn[25]	Carcinomatous metastases to bone,—multiple.	1+
Askanazy[17]	Lymphatic leukaemia	1
Decastello[18]	Acute lymphatic leukaemia	1
Decastello[18]	Chronic lymphatic leukaemia	7
Decastello[18]	Chronic myeloid leukaemia	13
Author's	Osteosarcoma,—single	5
Author's	Osteosarcoma,—multiple	1
Author's	Lymphosarcoma, multiple bone metastases	2
Author's	Melanotic sarcoma	1
Author's	Carcinoma breast, metastases to bone	4
Author's	Multiple enchondromata	2
Author's	Osteomyelitis	3
Author's	Osteomyelitis and periostitis,—luetic	1
Author's	Epiphysitis	1
Author's	Pyarthrosis,—knee	1
Author's	Arthritis,—knee, tuberculous	1
Author's	Rachitis	1
Author's	Osteitis deformans	1
Author's	Fracture	2
Author's	Acute lymphatic leukaemia	2
Author's	Chronic lymphatic leukaemia	1
Author's	Pernicious anaemia	3
Author's	Lead poisoning	1
Author's	Chronic myeloid leukaemia	1
		65+

A brief scrutiny of this table makes it apparent that extensive bone and bone marrow disease may exist unassociated with Bence-Jones proteinuria.

If we may assume from qualitative tests alone that the protein found in our own and the other cases collected, is identical with that excreted in myelomatosis, then any possibility of the Bence-Jones body being a specific derivative of a specific pathological process must be abandoned. In fact, the evidence at hand points strongly to the origin of this body, as a product of endogenous metabolism, rather than directly from the diseased tissue.

Notwithstanding the paradoxical incidence of Bence-Jones proteinuria in bone marrow disease, we cannot avoid the conclusion that the marrow is in some way concerned in its production. So far, there is very little experimental evidence bearing on this point. From certain digestion experiments Rosenbloom[27] draws the conclusion that Bence-Jones protein may be derived from osseoalbumoid (Hawk and Gies[28]). Zülzer[29] has shown that in dogs, repeated injections of pyrodin may produce a severe, "pernicious" anemia with hyperplasia of the bone marrow and the excretion of Bence-Jones protein in the urine. Again, as has been shown by Selling[30] the injection of benzol in rabbits induces a severe anemia with aplasia of the bone marrow. We have examined the urine of six such rabbits over four to eight consecutive days without finding a trace of the Bence-Jones body.

While the metabolic studies are not wholly in accord, the more careful and extended observations seem to indicate that the excretion of this body is largely independent of the amount and kind of protein ingested. There is much to commend the suggestion of Hopkins and Savoy[31] that Bence-Jones proteinuria be viewed as an intermediary metabolic anomaly analogous to cystinuria and alkaptonuria, but occurring at a higher level. "This interruption might be due either to the positive influence of a toxin from the growth or to the loss of some normal function of the bone marrow." There is nothing in the postulate essentially incompatible with the diversity of pathological conditions associated with the excretion of this protein. It is possible that the bone marrow has some function in connection with the endogenous metabolism of proteins, which may be disturbed by any one of a variety of disease processes.

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FURTHER OBSERVATIONS ON THE CARCINOMA SKIN REACTION.*

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In 1910 Elsberg, Neuhof and Geist[1] proposed a skin reaction for carcinoma, which consisted in the subcutaneous injection into the forearm of 5 minims of a 20 per cent suspension, in normal salt solution, of washed human red blood corpuscles, obtained from a normal, healthy individual. Their work comprised 684 injections in 432 patients, and an analysis of their cases shows a characteristic reaction in 89.9 per cent of the cases suffering from carcinoma, and no reaction in 94.3 per cent of non-malignant cases.

Moss,[2] following the work of Landsteiner, was able to show that every human being will fall into one of four isoagglutinin and isohemolysin groups, and that this grouping is established shortly after birth, and does not vary through life, in health or in disease.

This suggested the possibility that there was a relation between the skin reaction above described and the presence of normal isohemolysins. Were such the case, the value of the test from a specific diagnostic standpoint would be nil. In order to test this point, Gorham and Lisser[3] made a determination of the grouping of a large number of patients, and injected each patient with red blood cells belonging to each of the four agglutinin groups. Thus a ready comparison could be made between the reaction in *vivo* and in *vitro*.

Although their results indicated that apparently no connection existed between a positive skin reaction and hemolysis in the test tube, yet they determined the significant fact, that the grouping of the corpuscles employed for the injection is not a matter of indifference, but one of essential importance, since positive reactions occasionally occurred with one or two of the corpuscle groups, and not with the others. It was evident then, that the injection of an unknown group of corpuscles might lead to an erroneous deduction. However, there appeared to be one group, namely Group IV, (the corpuscles of which are neither agglutinated nor hemolysed by any sera in *vitro*), which might be utilized for the reaction with reasonable reliability, since in their entire series of 124 cases, in which the four types of corpuscles were injected subcutaneously, not a single instance was observed in which the corpuscles of Group IV gave a positive reaction without the corpuscles of Groups I, II, and III also showing a positive reaction.

Accordingly, in the hope of simplifying the test and shedding further light on its value in the diagnosis of malignant disease, we carried out another series of experiments, using the corpuscles of Group IV alone. This paper reports the results of the method in 62 verified cases of malignant disease (carcinoma and sarcoma) and in 94 cases of healthy individuals or patients suffering from various non-malignant ailments.

Technique.

The corpuscles used for injection were always obtained from the same individual, a normal healthy person under constant surveillance and definitely known to belong to Group IV. On the day before the tests were to be made, 15 cc. of blood were aseptically removed from a vein of the forearm and immediately introduced into sodium citrate, to prevent clotting. It is important to wash out the syringe with sodium citrate before use, in order to prevent any hemolysis from water left in the syringe after boiling. The corpuscles thus obtained were centrifugalized, the supernatant fluid pipetted off, and the cells washed three times with normal salt solution. A 20 per cent suspension was then made and allowed to remain over night in the ice chest. The next morning this suspension was drawn up into syringes which had been sterilized, and washed out with normal salt solution. The flexor surface of the forearm of the patient to be tested was cleaned with alcohol and ⅓ to ½ cc. of the corpuscle suspension injected subcutaneously. The corpuscles used were never more than twenty four hours old.

* From the Clinics of The Johns Hopkins Hospital.
[1] Am. J. M. Sc., 1910.
[2] Johns Hopkins Hosp. Bull., 1910, XXI, No. 228.
[3] Am. J. M. Sc., 1912, CXLIV, 103.

TABLE I.

VERIFIED CASES OF MALIGNANT DISEASES

No.	Diagnosis	How verified	Reaction		No. tests	Cured	Remarks
			Before operation	After operation			
1	Cancer of cervix	Operat'n and microscope.	+	..	1	?	
2	Cancer of cervix	Operation	..	?	1	?	
3	Cancer of cervix	Operation	..	0	1	Probably cured.	
4	Cancer of cervix	Operation	+	..	1	?	
5	Cancer of cervix	Operation	..	+	1	Not cured.	
6	Cancer of cervix	Operation	..	0	1	Probably cured.	
7	Cancer of cervix	Operation	0	..	1		
8	Sarcoma of bladder with metastases.	Operation	..	+	1	Not cured.	
9	Cancer of bladder	Operation	+	..	1	Not cured.	
10	Cancer of bladder	Operation	+	0	2	Probably cured	Positive April 29th, negative May 27th, after radical operation.
11	Cancer of bladder	Operation	..	+	1	Inoperable.	
12	Cancer of ovary	Operation	..	0	1	Questionable cure.	
13	Cancer of ovary	Operation	..	+	1	Inoperable.	
14	Cancer of rectum	Operation	+	..	1	Not cured.	
15	Cancer of prostate	Operation	..	+	1	Not cured.	
16	Cancer of prostate	Operation	0	..	1	Not cured.	
17	Cancer of prostate	Operation	+	..	1	Not cured.	
18	Cancer of prostate	Operation	..	0	1	Not cured.	
19	Cancer of cecum	Operation	..	00	2	Probably cured.	
20	Cancer of hepatic flexure	Operation	+	..	1	Not cured.	
21	Cancer of pancreas	Autopsy	+	..	1	Dead	Not operated on.
22	Cancer of pancreas	Operation	..	0	1	Inoperable.	
23	Cancer of stomach	Operation	+	..	1	Inoperable.	
24	Cancer of stomach	Operation	0	..	1	Not cured.	
25	Cancer of stomach	Autopsy	0	..	1	Dead.	
26	Cancer of stomach	Operation	+	..	1	Inoperable.	
27	Cancer of stomach	Tissue from gastric lavage	+	..	1	Not cured.	
28	Cancer of stomach with metastases	Clinically certain	0	..	1	Not cured	Not operated on.
29	Cancer of stomach	Clinically certain	+	..	1	Not cured	Not operated on.
30	Cancer of stomach	Operation	..	+	1	Inoperable.	
31	Cancer of stomach	Operation	..	+	1	Not cured	Gastro-enterostomy.
32	Cancer of stomach	Operation	+	..	1	Not cured	Gastro-enterostomy.
33	Cancer of tongue	Clinically certain	0	..	1		Not operated on.
34	Cancer of tongue	Operat'n (no microscope).	..	0	1	Possibly cured	Radical operation. Glands showed no cancer.
35	Cancer of lip	Operation	..	0	1	Probably cured	Radical operation two weeks before test.
36	Cancer of lip	Clinically certain	+	..	1	Not cured.	
37	Cancer of lip	Clinically certain	0	..	1	Not cured.	
38	Sarcoma of mouth	Operation	..	+	1	Not cured	Partial excision; inoperable.
39	Cancer of larynx	Laryngoscopic	+	..	1	Not cured.	
40	Cancer of tonsil	Autopsy	0	..	1	Not cured.	
41	Cancer of jaw	Operation	+	00	3	Probably cured	Radical operation.
42	Cancer of face	Operation	+	..	1	Not cured.	
43	Cancer of face	Operation	0	..	1	Not cured.	
44	Cancer of neck	Operation	0	+	2	Not cured.	
45	Cancer of breast (carcinomatosis).	Operation	+	..	1	Not cured.	
46	Cancer of breast	Operation	..	0+	2	Not cured	Recurrence 4 wks. after operation. Second test 5 wks. after operation.
47	Cancer of breast	Operation	..	+	1	Not cured	
48	Cancer of breast	Clinically doubtful	+	..	1		Subsequent history unknown. No operation.
49	Cancer of breast	Operation	..	0	1	Probably cured	Complete operation.
50	Cancer of breast	Operation	?	..	1	Probably cured	Complete operation.
51	Cancer of breast	Operation	+	..	1	Probably cured	Complete operation.
52	Cancer of breast	Operation	+	..	1	Died on table.	
53	Peritoneal carcinosis	Operation	0	..	1	Inoperable.	
54	Sarcoma of ribs	Operation	+	00	3	Possibly cured	No signs of recurrence 2 months after operation.
55	Cancer of spine	Operation	+	..	1	Not cured	Metastases from breast previously removed.
56	Cancer of bones	Autopsy	+	..	1	Dead.	
57	Sarcoma of ilium	Operation	00	..	2	Inoperable.	
58	Sarcomatosis	Autopsy	+	..	1	Not cured.	
59	Perithelial sarcoma	Operation	0	..	1	Not cured.	
60	Sarcoma of perineum (melanotic).	Operation	0	0	2	Not cured.	
61	Sarcoma of tibia (metastasis to groin).	Operation	..	0	1	Not cured.	
62	Retroperitoneal tumor	Operation	+	..	1	Not cured.	

TABLE II.

CASES OF NON-MALIGNANT DISEASE AND NORMAL CONTROLS.

No.	Diagnosis.	Reaction.	No. tests.	Remarks.
1	Typhoid fever	0	1	
2	Typhoid fever	0	1	
3	Typhoid fever	0	1	
4	Syphilis of liver	0	1	
5	Pernicious anaemia	0	1	
6	Pernicious anaemia	0	1	
7	Pernicious anaemia	0	1	
8	Secondary anaemia	0	1	
9	Diabetes mellitus	0	1	
10	Myelogenous leukaemia	0	1	
11	Myelogenous leukaemia	0	1	
12	Enlarged liver	0	1	Clinical diagnosis cancer of stomach. Exploration showed enlarged liver (luetic).
13	Enlarged liver	0	1	Clinically cancer or aneurysm. Explorat'n showed enlarged liver.
14	Cardiac disease	0	1	
15	Cardiac disease	0	1	
16	Cardiac disease	0	1	
17	Chronic nephritis	0	1	
18	Osteoarthritis of hip	0	1	
19	Arthritis of hip (tuberculous)	00	2	
20	Arthritis of shoulder (pneumococcus).	0	1	
21	Infectious arthritis (secondary anaemia).	+	1	
22	Gonorrhoeal arthritis (knee).	0	1	
23	Arthritis, sacro-iliac	0	1	
24	Osteoarthritis of hip	+	0	
25	Arthritis	0	1	
26	Ankylosis of hip	0	1	
37	Multiple arthritis	0	1	
28	Arthritis	0	1	
29	Relaxation of lumbar spine	0	1	
30	Spinal cord lesion (paralysis)	0	1	
31	Gastric ulcer	0	1	
32	Purpura	+	1	To be expected.
33	Gall-stones	+	1	Operation.
34	Gall-stones	0	1	Clinically thought to be gastric ulcer with early carcinomatous change (operation).
35	Chronic pancreatitis and cholecystitis.	0	1	Operation.
36	Chronic appendicitis	+	1	Operation.
37	Acute appendicitis	0	1	Operation.
38	Appendix abscess	0	1	Operation.
39	Acute appendicitis	0	1	Operation.
40	Chronic appendicitis	0	1	Operation.
41	Subacute appendicitis	0	1	Operation.
42	Chronic appendicitis	0	1	Operation.
43	Intestinal obstruction	0	1	Operation.
44	Renal calculus	0	1	Operation.
45	Pyonephrosis	0	1	Operation. Thought to be a hypernephroma.
46	Hernia	0	1	
47	Hernia	0	1	
48	Hernia	0	1	
49	Hernia	0	1	
50	Hernia	0	1	
51	Hernia	0	1	
52	Hernia	0	1	
53	Hernia	0	1	
54	Hernia	0	1	
55	Hernia	0	1	
56	Hernia	0	1	
57	Hernia	0	1	
58	Hernia	0	1	
59	Hernia	0	1	
60	Hernia	0	1	
61	Hydrocele	0	1	
62	Hydrocele	0	1	
63	Varicocele		1	
64	Varicocele	0	1	
65	Benign hypertrophy of prostate.	0	1	Operation.
66	Benign hypertrophy of prostate.	0	1	Operation.
67	Benign hypertrophy of prostate.	0	1	Operation.
68	Vesical calculus	0	1	Operation.
69	Perirectal abscess	0	1	
70	Perirectal abscess	0	1	
71	Perirenal abscess	0	1	
72	Chronic infection of leg	0	1	Anaemia and cachexia.
73	Chronic infection of leg	0	1	
74	Carbuncle	00	2	
75	Old fracture of tibia	0	1	
76	Compound fracture of tibia	00	2	
77	Fracture of patella	0	1	
78	Fracture of radius	0	1	
79	Deformed leg	0	1	
80	Club foot	0	1	
81	Ulcer of leg (benign)	0	1	Microscopic examination.
82	Contusion of arm	0	1	
83	Osteomyelitis of clavicle	0	1	
84	Burn of arm	+0	2	Positive shortly after being burnt.
85	Tuberculosis of breast	+	1	Clinically and at operation cancer. Microscopically showed tuberculosis.

TABLE II.—*Continued.*

CASES OF NON-MALIGNANT DISEASE AND NORMAL CONTROLS.

No.	Diagnosis.	Reaction.	No. tests.	Remarks.
86	Mixed tumor of parotid	0	1	Before operation.
87	Polypoid endometritis	0	1	Clinical diagnosis uncertain.
88	Aneurysm	0	1	
89	Aneurysm	0	1	
90	Pigmented mole of face	0	1	
91	Lipoma of axilla	0	1	Before operation.
92	Control	00000	5	
93	Control	0000	4	
94	Endocervicitis	+	1	Operation.

REACTION.

When the injection is properly given a small tumor at once appears, which soon subsides, leaving a pin point abrasion where the needle entered. The reaction begins to appear, as a rule, between three and five hours after the injection, gradually increasing in intensity until it has reached its height at the end of six to eight hours. When fully developed, it appears as a somewhat irregular oval area, measuring from 1×2 to 3×5 cm., with a well-defined margin. The color varies from a brownish red to a maroon, with frequently a bluish to purple tinge. The lesion is distinctly raised from the surrounding skin, slightly boggy on palpation, and often somewhat tender. When the lesion has disappeared, there remains behind a flat, yellowish, or greenish, discoloration, such as is left by any ecchymosis. Negative cases show either the point of needle puncture or a small flat area of varying color. It is advisable to give injections early in the day so that observations by daylight are possible.

MISLEADING REACTIONS.

1. *The Intradermal Reaction.*—Care should be taken to give the injection under the skin, and not into it. Confusion may occur otherwise, since a peculiar indurated, reddish lesion will usually result. This, however, can be readily distinguished from the true positive test.

2. *The Immediate Reaction.*—In choosing the site for injection, one should be careful to avoid superficial veins. Yet, in spite of exercising this precaution, a few cases will at once show an area of purplish discoloration. This must never be considered a positive reaction—and, usually, the giving of another injection in another location will correct the error. Occasionally, however, even though no tiny vessel has been ruptured, a reaction will occur at once, apparently without explanation.

3. *The Painful Arm.*—In eight cases, there appeared within eight to ten hours a diffuse reddening of the skin about the site of the injection, covering an area of 3×6 inches, which became redder in the next twelve hours, reaching a maximum in about twenty-four hours. The arm then was red, hot, tender, and there was considerable pain on motion at the elbow. The symptoms disappeared gradually in the next twenty-four hours, leaving no ill effects. There was no general reaction. Infection seemed to be safely excluded since the great majority of patients injected in precisely the same manner, at the same time, with the same suspension,

showed absolutely no such result. An anaphylactic phenomenon was thought of, but this peculiar picture still remains unaccounted for.

Summary.

A. verified cases of malignant disease tested before operation or after a palliative operation.

Positive reactions	37	66%
Negative reactions	19	34%
Total cases	56	

In three of these patients tested as controls, where malignancy had not been suspected, the appearance of a positive skin test was followed in each case by exploration and the disclosure of the presence of cancer.

B. verified cases of malignant disease tested after an operation supposed to be curative.

Positive reactions	0	0%
Negative reactions	10	100%
Total cases	10	

With regard to the prognostic significance of the test, it is interesting to note that in the small series of cases (ten) tried after supposedly curative operation, not a single positive reaction occurred. It is important, however, to determine more completely just what indication the test affords of the recurrence of cancer after a radical operation. In one case, for example, (No. 46) there was a negative reaction immediately after a complete excision of a cancer of the breast. A week after the indications of recurrence, which appeared a month after operation, the test was positive.

C. non-malignant cases giving positive reactions.

1. Infectious arthritis with secondary anæmia.
2. Osteoarthritis of hip.
3. Gall stones.
4. Chronic appendicitis.
5. Tuberculosis of breast.
6. Endocervicitis.
7. Burn of arm (in early toxic stage).
8. Purpura.

The last two could be excepted, but even including these, results show

Positive reactions	8	8.4%
Negative reactions	86	91.6%
	94	100.0%

In considering the specificity of the test, the question naturally arose as to whether the positive reactions were not due to the cachexia and toxæmia coincident with the malignant disease. To settle this point a number of individuals were selected who were in advanced cachexia from chronic infections, or affected with diseases in which presumably blood destruction was going on, such as pernicious anæmia and leukæmia. These cases were all negative.

Conclusions.

A summary of the above 158 cases, in which corpuscles of Group IV alone were used show that:

1. In 62 cases of verified malignant disease, two-thirds gave a positive reaction, and one-third were negative.
2. In 94 control cases, 91.6 per cent were negative and 8.4 per cent positive.
3. As a practical diagnostic adjunct, a negative skin test adds little or no weight to the evidence against cancer, being comparable to many other clinical tests of empirical nature.
4. A positive reaction is strong presumptive evidence of cancer.
5. To obtain reliable results, corpuscles of Group IV must be used.

ON THE CAUSES OF BIRTH.

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One of the most interesting series of problems is that associated with the reproductive function in the female: the relation of ovulation to menstruation; the physiology of implantation; the "selective function" of the fetal membranes and placenta; the embryo metabolism and its influence upon the mother; the causes of birth; the origin of the stimulus for the first respiration; the physiology of the fetal circulation and its relation to the changes at birth; the influence of the internal secretion from the ovary and particularly the function of the corpus luteum; and perhaps along with these the factors in the determination of sex. Preyer[1] was probably the first to take up the study of problems of this character in a systematic way, and Marshall[2] in his recent book on "The Physiology of Reproduction" has brought the greater part of the literature together in an accessible form. It is not the writer's intention to attempt a solution of the causal factors in the parturient act but rather to give some idea of what has been done together with some suggestions as to the unexplored phases in the question.

Hippocrates,[3] some centuries before Christ, realized that some fundamental cause must underlie the birth of the child and dismissed it about as follows: that as the embryo grew, its demand for nourishment became greater than the source of supply could furnish, and finally, driven by hunger, the child pushed its feet against the fundus of the uterus and forced its way into the outer world. This naive explanation was questioned by Galen[4] who first described the uterine contractions and held them responsible for the expulsion of the

child. Galen maintained that the "fetus was retained in utero until sufficiently grown and nourished to take food by the mouth" (after Harvey) and "that uterine contractions plus the additional pressure through the abdominal muscles were responsible for birth" (after Knüpffer). Fabricius,[5] some fifteen centuries later added another suggestion "that the weight of the fetus becomes so great as to exert considerable pressure, and the bulk such that the uterus is unable to retain it, added to which the quantity of excrementitious material is so much increased that it cannot be contained by the membranes" (after Harvey).

Harvey[6] entered a general objection to the hunger and the cooling-off theories of Galen in no uncertain language. He asked the following question: "How does it happen that the fetus continues in the mother's womb after the seventh month? Seeing that when expelled after this epoch, not only does it breathe but without respiration cannot survive one little hour, whilst, as I before stated, if it remain in utero, it lives in health and vigor more than two months without the aid of respiration." This question is the most important one asked in the history of the problem and is worth no little consideration. Harvey went on to show that the "uterine humors were not excrementitious"; that the weight and the bulk of the uterine contents were not causal factors in starting contractions; and that the activity of the child itself did not afford the necessary stimulus. "I should rather attribute the birth of the child to the following reason—that the juices within the amnion, hitherto admirably adapted for nutriment, at that particular period either fail or become contaminated with excrementitious material."

Harvey's essay on parturition, like his description of the fetal circulation, was a result of careful study and not mere speculation. He saw the problem in its wider aspects and brought forth the development of the bird to show that it was not hunger but rather the need of respiration that drove the chick from its shell. Just as Harvey's views have been neglected in the bibliographies on the problem, so the epoch-making discovery of his contemporary, Mayow, has not been seriously considered. Mayow[6a] in his argument on the respiration of the fetus calls attention to the fact that "the embryo in its membranes seems to be nearly in the same case and to breathe in very much the same manner as the chick enclosed in the egg. If, however, the fetus is stripped of its membranes, and contracts the muscles of the chest and the diaphragm, there is now a greater expenditure of nitroaerial particles for muscular effort, and consequently the fetus is under a greater necessity to breathe, since nothing is any longer received to supply the want of respiration." The reader must judge for himself whether or not a knowledge of the oxygen of Priestley (a century later) was essential to a true understanding of what respiration meant.

Some forty years after the publication of Harvey's essay, Mauriceau[7] "re-discovered" the distension theory of Fabricius and clearly disregarded Harvey's excellent objections to the same. The distension theory remained as such until about a century later when Petit and Baudeloque attempted to better it. Petit[8] concluded that the uterus might be considered completely distended when the cervical canal became incorporated in the uterine cavity, and when this room had been taken up, the uterus contracted. This was again somewhat modified by Baudeloque[9] who proposed that the uterus was inherently an organ of contraction and attempted to rid itself of the fetus from the first but was prevented by the cervix. When distension, however, had overcome the cervical rigidity, the muscular contraction became effective. Reil[10] changed the view of Baudeloque and while he regarded the uterus as an inherently contractile organ, considered that the distension overcame the contractile power until an irritant limit was attained when the uterine contractions were initiated.

Naegele[11] in 1812 again modified the view of Baudeloque and Reil by including the hypothesis proposed by Hippocrates that the fetus outgrew its source of supply. He maintained that the connection between the fetus and the mother became progressively less as gestation went on until finally the union was dissolved and the fetus, acting as a foreign body, set up contractions in the uterus. This brought into prominence a theory known as the foreign-body theory in our present literature. Power,[12] Hoffmann,[13] Hayn,[14] and Dubois,[15] saw an importance in an analogy which they declared existed in the function of the pelvic organs and advanced the similar notion that just as the urinary bladder was stimulated to contract so the uterus, following the distension theory, expelled the fetus. Hoffmann went so far as to propose that the ovary represented a gland, the tube a duct, and the uterus a sort of bladder. Carus[16] again brought up the distension theory in 1839 and like Baudeloque and Reil found the uterus to be primarily a contractile organ. He placed the time of birth at the period where the uterine musculature became completely developed.

Mende[17] in 1821 made the excellent suggestion that the causal factor lay outside of the uterus and regarded the stimulus as derived through the tenth menstrual period. While Joerg[18] in 1831 again brought up the foreign-body theory and modified it in a somewhat remarkable way. He considered that distension of the uterus brought about an interference with the abdominal circulation in such a way that the circulation in the uterus itself was hampered, with consequent degeneration of the membranes and dissolution of the connection between mother and child. Litzmann[19] defined the uterus as the organ of birth, and was the first to call attention to the fact that the fetus was sometimes developed in other places—a point of some little importance which was overlooked even by later writers. He believed that the contractions were initiated through the nervous system and looked upon the complete development of the nervous mechanism as a determining factor in the cause of birth. Kilian,[20] Scanzoni,[21] Hohl[22] and Tyler-Smith[23] did not contribute materially to what was known except possibly the latter who, favoring the theory of Mende, regarded parturition as a sort of cumulative menstruation. Kilian leaned toward the foreign-body theory; Scanzoni saw the importance

of pressure upon the sensory terminals of the uterine nerves; and Hohl anticipated the natural selection theory by regarding the complete development of the fetus concomitant with that of the uterine musculature.

Up to the year 1858 practically no experimental work had been done on the problem and the solutions offered were largely matters of conjecture supported in part by clinical evidence. Brown-Sequard[24] was the first to perform experiments and found that the uterine musculature became more irritable as gestation advanced and that overloading the maternal blood with CO_2 brought about uterine contractions. That Brown-Sequard was ahead of his times is indicated by the fact that Spiegelberg,[25] Eichstedt,[26] Obernier,[27] and Kehrer[28] published later and based their work on conjecture. Eichstedt suggested that the fetus determined the time of birth by swallowing the amniotic fluid, thereby creating a negative pressure in the uterus. The others did not advance an idea which might be termed original. Reimann[29] suggested the possibility of a nerve center which inhibited the uterine contractions and believed that direct stimulation to the uterus or depression of the inhibiting center might bring about the birth act.

The ten years from 1870-1880 were characterized by actual researches and the names of Friedländer,[30] Simpson,[31] Kundrat and Engelmann,[32] Leopold,[33] and Runge[34] may be mentioned. The last named checked the experiments of Brown-Sequard, while the others were interested primarily in the structure of the placenta. Friedländer discovered evidences of thrombosis in the placental sinuses during the eighth month of gestation and this was substantiated by Leopold who called particular attention to the venous congestion and the signs of extravasation. Simpson claimed a fatty degeneration of the membranes which was substantiated by Kundrat and Engelmann but held inconstant by Leopold. Runge, following the experimental line of work, discovered that while excesses of CO_2 stimulated the uterus, withholding O brought about the characteristic tetanic contractions.

In 1881 Hasse,[35] following the idea that an excess of CO_2 was responsible for uterine contractions, proposed that the CO_2 excess was developed in the placental sinuses by reason of a gradual change in the mechanics of the fetal circulation. He also suggested that an excess of waste products might be held in part responsible. Hasse's suggestion regarding a change in the fetal circulation has not been accepted and as Blumreich[36] pointed out even if there were excesses present in the fetal blood stream it would be difficult to show that they would affect the uterine muscle which has nothing to do with the placental sinuses. Geyl[37] in 1881, influenced by Darwin, saw an importance in natural selection as the determining factor; a matter already hinted at by Hohl in 1855. Boehm[38] later practically agreed with the theory offered by Geyl and believes that it is the most reasonable explanation. Liedke[39] expressed an interest in the effect of urea upon the uterine musculature but whether or not he followed this research the writer has been unable to ascertain.

Minot[40] in 1889 revived the influence of the tenth menstrual cycle proposed by Mende and later by Tyler-Smith. Minot regarded menstruation and parturition as homologous and that parturition is a sort of cumulative menstruation. Keilmann[41] in 1891 again brought up the irritation of the cervix theory and his work was followed by that of Knüpffer.[42] Both of these investigators found a development of a system of ganglion cells in the supravaginal portion of the cervix and agreed that it was a stimulation of these intrinsic ganglia which brought about the birth act. The irritability of the cervix had of course been known for many years and their findings were naturally supported by certain clinical data but as Veit[43] pointed out the supravaginal ganglia would not account for the false labor pains in extrauterine pregnancy.

Blumreich[l. c.] in an excellent review of the question, went into the experimental evidence in some little detail and found that none of the existing theories of the cause of birth were well grounded. He himself leaned strongly toward a mechanical or traumatic cause although he appreciated the weakness of his contention.

The work of the past fifteen years may be arranged into three general classes: the first is an exaggeration of the doctrine of cycles; the second bears on an internal secretory relation; and the third leans toward the theory of immunity.

Beard[44] was the first to call attention in a scientific way to the theory of cycles; the menstrual cycle and its relation to parturition had naturally been proposed before. Beard, however, assumed that the cycle in the ovary in man occupied 23 days+. He also brought forward what he termed "the critical period" in the development and this "critical period" represented a stage in the development where the embryo took on distinct characteristics of the species. In man he computed this "critical period" was to be found at a 46 day+stage in the development or double the ovulation period. The duration of gestation he claimed must be computed in terms of "critical periods" and not of menstrual periods and, therefore, the span of gestation in man was equal to six critical units and not to ten menstrual periods. Beard's hypothesis may be expressed in the following words: "The ovary, with its nervous apparatus, from the moment of puberty to the time when its functions naturally cease, may, indeed, be compared to a clock, wound up at the start, and striking the hours with extreme regularity by the periodic emission of one or more eggs. During pregnancy, the clock does not cease to run; it still strikes the hours but in a muffled fashion so that, if all goes well, the sound is not heard outside of the ovary. And, just as some clocks are so arranged, as to give an indication of the striking period, so the ovary announces the normal advent of birth some little time before the ovulation due soon after the birth period." This explanation, therefore, assumes that the period of gestation must run in cycles predetermined by the cycle of the ovary and curiously enough Beard hit upon a 23 day cycle for the female while Fliess[45] found this to be the cycle in the male.

Like Pythagoras, Fliess found magic in numbers, and developed a *Weltanschauung* in a book that is quite beyond

the writer. According to him all things are governed by cycles; in the male, 23 days; in the female, 28 days; and in hermaphrodite forms, 17 days. It may perhaps be well to regard the work as a personal equation of Fliess' until someone well oriented in metaphysics and mathematics has checked his data. The numbers 7, 11 and 6 seem to do equally well and the strange thing is that Beard claimed the periodic function of the ovary to be in terms of 23 days, not 28 days. Symptoms of this theory of cycles nevertheless seem to exist, and a number of interesting cases are reported by Swoboda.[46]

The second series of theories is that connected with a functional relation between ovary and uterus. Pflüger is credited with being the first to suggest a nerve connection although practically the same thing was advanced by von Rotterau[47] in 1852. Pflüger[48] looked upon menstruation as a sort of cumulative reflex touched off by the periodic congestion of the ovary, and an influence of the ovary on parturition, following the relation of menstruation to pregnancy, is not difficult to conceive. Pflüger's views on the relation of ovulation to menstruation or rather the relation of both of them to a congestion of the ovary were in the main supported by Leopold. Beard[l. c.] in 1897 was the first to point out a possible function for the corpus luteum which he regarded as a follicle modified to suppress ovulation during gestation. Born[48a] in 1900 suggested that the corpus luteum was an organ of internal secretion and the first article on this side of the question is by Fränkl and Cohn[49] in 1901. Much literature has appeared since this time by Fränkl,[50] Marshall,[l. c.] Loeb,[50a] Steinach[51] and others. This internal secretory relation, however, brings up the question of the relation of ovulation to menstruation or a common cause in a third factor. As far as offering an internal secretion of the ovary or a relation between the internal secretion of the ovary and the fetus as a cause of birth, nothing very definite is at hand.

Since 1900 there has been a growing tendency to regard the relation between fetus and mother as a purely biochemical one and this naturally falls outside of the province of the anatomist. Thenen[52] in 1900 proposed a refinement of the Baudeloque theory in that he considered the active agent in inhibiting uterine contraction to be found in a vital principle (*vitaler Reiz*) located in the fetus and its membranes. Veit[53] in a rather exhaustive monograph developed the theory of toxicity of the chorionic villi and their behavior when transported in the maternal blood stream, and this seems to be substantiated by the recent work of Fieux and Mauriac[54] in the demonstration of a specific antibody to the toxic qualities of the villi developed in the mother during the second and third months of gestation but disappearing during the fourth. Similarly Ermys-Roberts[55] proposed an enzymic action of the ovum to account for its implantation. Schaeffer[56] located the inhibitory influence to uterine contractions to be found in the syncytial tissue of the placenta and also suggests the lowering of a resistance in the maternal blood at the time of birth. Healy and Kastle[57] found a hormone in the breast which gives rise to uterine contractions—a chemical relation between breast and uterus, therefore, and not a nervous mechanism. The evidence, in other words, points strongly toward the possibility of the embryo determining its own ripeness in terms of altered metabolism or specific influence which may touch off the uterine contractions. It is, however, well known that uterine contractions may be set in operation from the maternal side but this may be regarded a contributing factor as Goltz's experiments on the dog would indicate.

Moenkhaus[58] showed that hybridization increases the period of development and his experiments on fish seem to indicate that the sperm cell exerts a toxicity on the egg cell and may be responsible for the inhibition noted. Similarly Steinach found undoubted evidences of an antagonism of the internal secretion of the testis and the ovary in an inability to make ovarian grafts "take" in a male animal unless it be castrated. Perhaps this toxicity of the male influence upon the female may sometime be held accountable for the relatively larger number of male abortions.

Little work has been done on the causal factors in the hatching of the chick excepting perhaps the work of Preyer on the interchange of gases and the marked rise in the demand for oxygen just before the respirations set in. Recently Keibel[59] has found an interesting functional adaptation on the part of chick and duckling in a marked hypertrophy of the complexus muscle just before the hatching; the development of this muscle permitting a more effective use of the "egg-tooth." The same lack of any very definite information is found in the literature on the viviparous reptile and fish. In the former as far as we are aware only a gaseous interchange occurs and yet the garter-snake brings forth her young intact in the membranes "when they are sufficiently developed." It is, therefore, not likely that we can solve the question of the causal factors in birth until we have more facts and until the process is understood in lower forms where the relations are relatively simple. The case reported by Chapman[60] is suggestive. On October 16, 1816, a woman gave birth to what Chapman terms a 5-6 months' placenta and membranes and a 3-4 months' enclosed fetus; on December 10, 1816, she gave birth to a full term child! Objections may be made to any one theory or combination of theories proposed and until we can answer the question proposed by Harvey, why the embryo remains in the uterus after the seventh month, we cannot assume that much is known of the causes of birth.

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MORBIDITY AND MORPHOLOGY.

A COMPOSITE STUDY OF THE INCIDENCE OF DISEASE AND PHYSICAL FORM IN NEW ORLEANS, LOUISIANA.

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My studies of the Filipinos while I was living in the Philippines from 1907 to 1910 enabled me to classify the natives into three large general groups, depending upon their form of head, face, nose, ears, trunk and extremities. Before leaving the archipelago I associated tuberculosis with one of the groups and kidney diseases with the other two. My studies included more than 500 diseased individuals chiefly in the town of Taytay, about 30 miles from Manila, where a medical and anthropological survey was conducted under the direction of the Bureau of Science of the Philippine Government. More than 100 post mortem examinations were subsequently made at Malecon Morgue and the work done at Taytay on the living was in this way corroborated.[1]

Investigations have been continued from time to time since then in New Orleans at the Charity Hospital and the Touro

[1] The results of these observations may be found in my work (Chapter VII) The Racial Anatomy of the Philippine Islanders, J. B. Lippincott Co., Philadelphia, Pa., 1910. The terms used there, Iberion, Austreloid and Primitive, are here replaced by hyper-onto-morph, meso-onto-morph and hypo-onto-morph, respectively.

Infirmary Dispensary, where more than 1000 individuals have been examined. In addition to this about 100 post mortem examinations were made. My work was accomplished chiefly through the kindness of Dr. Lemann, at the Touro Dispensary, whose clinic I attended during the spring months, March, April and May, of 1911 and 1912. I examined first the general morphology of the patient and later examined the case medically with Dr. Lemann or someone else, the diagnosis being concurred in by at least two physicians.

Only 894 of the 1000 records obtained are utilized in this study because of the absence of essential data in the remainder. Diagnosis was made of 539 diseases among the 490 colored individuals, and 445 diseases among the 404 white individuals. When it is understood that 127 negroes and only 24 whites have constipation and in the majority of these there is no other affection, it is demonstrated that the whites exhibit a slightly greater relative morbidity than the blacks, but in none of these figures are the facts significant.

It may be of interest to note the incidence of diseases and sex. One hundred per cent more men than women have tuberculosis, whereas one hundred per cent more women than men have diseases of the central nervous system. One hundred per cent more men than women have syphilis and accidents are more frequent among men than women. On the other hand there is more anemia and constipation among women than among men. These differences may be incidental to habits, or merely accidental variations, without significance.

The white and colored elements of the hospital population here represented exhibit evidences of morbidity in different directions, as indicated in the following table, in percentages.

TABLE I.

White Morbidity Predominant.

	Pulmonary Tuberculosis	Nervous System	Digestive System	Arthritis	Emphysema	Anemia
White ..	19	13	5	5	3	3
Colored .	9	5	2	1	1	0.2
Total ...	14	9	4	3	2	2

Colored Morbidity Predominant.

	Constipation	Venereal	Cardiac and Renal	Pleurisy	Aneurysm	Asthma	Trauma
White	5	11	8	1	1	0.6	3
Colored ...	25	23	10	2	2	1	4
Total	15	17	9	2	2	1	4

Others.

	Acute Infections	Arterio-Sclerosis	Others
White	10	4	10
Colored	10	3	4
Total	10	4	7

It is to be seen from this table that the whites have more pulmonary tuberculosis, diseases of the nervous and digestive systems, arthritis, emphysema and anemia, whereas the blacks have more constipation, venereal diseases, diseases of the cardiac and renal systems, pleurisy, aneurysm, asthma and traumatic affections, the two having about an equal share of infectious diseases and arterio-sclerosis. The whites have the most of the remaining diseases.

The differences noted are of interest because of the differences in morphology and cultural conditions of the two peoples. The excess of constipation among the colored people is not necessarily an indication of greater susceptibility on their part, but represents their greater ignorance regarding the value of keeping the bowels open and the use of proper means to secure that effect. Neither can the greater extent of venereal infections among the colored people be attributed to greater susceptibility on their part, because the extent of venereal infections among a people is considered to be due directly to the freedom of sexual intercourse—promiscuity. We may infer, therefore, that greater freedom exists among the negroes than among the whites, which condition is acknowledged to be true by all competent observers. So prevalent is venereal infection among them that the question asked the colored people in taking histories in the New Orleans hospitals is not "Did you ever have" the infection, but "When did you have" it.

There are two significant conditions, however, that indicate structural or physiological differences rather than differences in cultural conditions. These are that the whites have more affections of the lungs, of the nerves and of the alimentary canal, whereas the blacks have more affections of the circulatory and renal systems. These differences may be attributed by some observers to physiological causes and may be due to occupation, habit, or other activities of body or mind. One may say that the heart, arteries, veins and kidneys of the colored people are more susceptible to disease than other parts of the system because of the greater stress of manual labor and the excessive sexual exertion on their part; whereas, the brain, nerves, stomach, intestines and lungs of the white people are more susceptible to disease because of greater mental activity and sedentary occupations. The out-of-door activity of the negroes in laborious occupations involving stress and strain of the connective tissue structures undoubtedly produces a greater number of traumatic cases, may affect the heart and kidneys and possibly induces a relative freedom from tuberculosis. But there are fundamental differences in morphologic structure that may account for these differences in susceptibility of the two peoples, and the differences in structure are based on the two fundamental embryonic tissues, mesothelium and epithelium; the lungs, nervous system and alimentary canal derived from epithelium, the heart, circulatory system and kidneys derived from mesothelium. Certain types regardless of race, color, or cultural conditions may be called mesothelial types, while others equally distinct may be called epithelial types. The mesothelial types are greatly developed in bone, muscle and other connective tissues, whereas the epithelial types are less developed in this way, are more developed in brain, lungs and alimentary canal. Great development of either class of tissue seems to weaken it and make it more liable to disease, therefore the two types may be called *epitheliopath* and *mesotheliapath*. The latter is the meso-onto-morph, the former the hyper-onto-morph. But I am going ahead of my subject.

While in the Philippine Islands, I noticed a difference in

susceptibility after I had segregated the types. This occurred in the following way. All unclaimed bodies in the city of Manila are brought to the morgue connected with the medical department of the University of the Philippines where they may be utilized for anatomical purposes. I selected the thin subjects for dissection for two reasons, because they dissect with greater ease and they take injections better. On examination it was found that they had usually died of pulmonary tuberculosis, their arteries were elastic and free from signs of arterio-sclerosis, and their connective tissues, muscle and bone were poorly developed and fragile. Such subjects were invariably of the hyper-onto-morph form, the epithelial type, the epitheliopath. At that time I associated the type with susceptibility to tuberculosis, but since then I have found that all the epithelial structures seem to be more liable to disease. The meso-onto-morph on the other hand is more liable to diseases of the mesothelial tissues.

One unexpected feature of the two forms is that the hyper-onto-morph has a short intestine, 12 to 15 feet, whereas the meso-onto-morph has a long intestine, 20 to 25 feet. I have frequently amazed my students by predicting the length of the intestine before the body was opened, which I did by previously examining the ears of the individual.

I have devised a system of descriptive morphology and have used it in racial anatomy to differentiate morphologic forms. The most exact anthropologists decree that nothing shall be accepted that is not exactly measured or defined, yet there are certain qualities which can be described more accurately than they can be measured. My work is on the order of zoölogy applied to man and is the method of the naturalist rather than the mathematician.

Man's form may be classified by means of the external ear, physiognomy and body parts in three fundamental physical forms. The three fundamental forms represent stages of evolution in the race as well as degrees of growth in the individual, and I have used the terms: hypo-phylo-morph, meso-phylo-morph and hyper-phylo-morph to designate three stages of the former and the terms hypo-onto-morph, meso-onto-morph and hyper-onto-morph to designate three degrees of the latter.

The hypo-onto-morph is usually small in stature and fat, with short legs and arms, chubby hands and feet, and relatively long trunk, the characteristic form of childhood predominating. The head is round, broad and short, and large in relation to the stature of the individual, the total head height from chin to vertex being 1/6 to 1/7 of the total stature, the normal for the European being about 1/8. The face is ovoid, with small forehead and chin, wide cheeks, and is very broad and short, often dished or depressed about the nose—flattened in front—and the face below the eyes is small compared to the size of the head, as in the infant. The nose is flat, broad and short, with depressed, flattened bridge, upturned tip, and the nostrils open forward rather than downward. The eyes are often narrow slits and the eyelids are "puffed" as if infiltrated. The cheeks appear as if they had chestnuts in them thus completing the infantile appearance. This form is found largely throughout the Orient and is a fundamental Malay or Mongolian type. Modified forms similar to this are found elsewhere, especially among the Africans and not a few among the Europeans.

The meso-onto-morph is of medium size and stockily built. The extremities are relatively long, the feet and hands large and the trunk is short. The head and face are ellipsoid, and large compared to the size of the head. The malar and zygomatic bones are prominent, the nose is massive, long, wide and high, with depressed root, straight bridge and nostrils that open downward and forward. This is the fundamental African form but is also found extensively in Europe where it has undergone modification, and it is not unknown in the Orient.

The hyper-onto-morph is either tall and slender or small and delicate. The trunk and extremities are intermediate in length between those of the other two, and the face is also intermediate in size and pentaganoid or triangular, with broad forehead and small chin. The total head height from chin to vertex is less in this form than in the other two, about 1/8 the total stature, the European artist's ideal. The head is large in proportion to the size of the face below the eyes. The head is long and narrow, and the nose is also long and narrow, with high root and bridge, and the nostrils open downward. The eyes are wide open and close together, in contradistinction to those of the hypo-onto-morph, which are semi-closed and far apart. This is the fundamental European form, although their dispersal through migrations, both historic and prehistoric, has taken them to almost all parts of the earth.

From the phyletic standpoint the European represents the present day product of what was originally the hyper-phylo-morph, although occasional mixtures with the hypo-phylo-morph and the meso-phylo-morph have occurred. The African represents the meso-phylo-morph in the same way, and the Oriental the hypo-phylo-morph, each having mixed to some extent with the other two forms.

The terms hypo-, meso-, and hyper-phylo-morph might have been retained instead of using the terms hypo-, meso-, and hyper-onto-morph but I preferred the latter as more specific and because they refer to individuals rather than peoples. The hyper-onto-morph, etc., is then the living representative individual of what was once the hyper-phylo-morph, etc., and retains the original form to some extent, but may have black skin and kinky hair among the negroes, black skin and straight hair among the East Indians, ruddy skin, blonde hair and blue eyes among the North Europeans and tanned skin, black hair and dark eyes among the South Europeans or Mediterranean peoples. In other words I believe the form to be more fundamental than the pigment or hair structure.

It cannot be denied that forms similar to those described under the three heads hypo-, meso-, and hyper-onto-morph may be due to the effects of individual development, or the environment during one generation, in other words, ontogeny, but in general I believe the three forms are relics of previous phyletic forms. Individuals may also be seen who have one

or more of the characters of one form, but otherwise are of one of the other two forms, and this may be attributed to mixing, but is more apt to be a matter of individual development—ontogeny.

The characteristics heretofore given are those usually described by morphologists, but my classification is based more upon ear form than any other factor. The form of the external ear, or pinna, should be more unchangable than any of the characteristics previously given because it is not so liable to physiological and selective influences, and because it is fundamentally cartilage, which, as the ground work for bone, should be the most stable of tissues.

The human ear may be described as consisting essentially of two parts, the external border, or helix, with its lower end, the lobule; and the central part, or concha, with the tragus and antitragus. The outer border of the concha is also the inner border of the helix and it is called the anthelix. The tragus is the small nodule immediately in front of the ear hole, or external auditory meatus, and the antitragus, which is opposite the tragus, is the lower end of the anthelix. Darwin's tubercle is to be seen on the upper part of the helix on the inside of its overturned margin near the top of the pinna. It represents the tip of the ear which has turned in towards the concha during the growth of the fœtus before birth. The pinna is at first formed flat in the embryo and at the fourth month of intrauterine life there is a tip at the upper outer margin of the helix. At this time the ear of the fœtus resembles that of the monkey, *Macacus rhesus*, with its pointed tip extending upward and backward. Later in the development of the fœtus the ear is reduced in size by the rolling in of the tip and of the entire helix, accompanied by a protrusion of the anthelix system including the tragus and the antitragus. When the adult human ear has attained its full maturity the rim of the helix has rolled inward and forward and the tip becomes Darwin's tubercle.

We may conceive that the first or earliest form of the ear after the fourth month of fœtal life is one in which the helix has rolled in, but the anthelix system, including the rim of the concha, the tragus and antitragus, has not projected far out from the head. In this condition the ear would have the form of a half bowl, and would be semi-trumpet shaped. This is the condition of the hypo-phylo-morph ear. Should the ear continue to develop it would assume the shape found in the hyper-phylo-morph, when the ear is flatter with the anthelix system at times projecting beyond the helix, and the latter turned backward towards the head. The tragus and antitragus would then project, and the lobule would be close to the head. The form of the meso-phylo-morph is somewhat intermediate between the other two, but is a distinct type nevertheless.

The hypo-onto-morph ear is usually small and round, the helix is turned in and forms a heavy roll at the rim of the ear extending downward into the lobule which turns almost horizontally to form a shelf-like lower border to the ear. The anthelix is almost parallel to the helix and is about the same size because the helix has rolled in until it has almost covered the anthelix, the two looking like a double roll surrounding the concha. The latter is deep and wide like a bowl or trumpet. The tragus and antitragus do not project beyond the helix but are turned in or depressed. The upper half of the helix turns over to form a shelf, like that of the lobule, and between the two is a part of the helix which does not project as much as the other parts. The hypo-onto-morph ear is usually thick and coarse, with rounded edges, and skin lines that are large and far apart, with large ridges between them.

The hyper-onto-morph ear stands in a contrast with the ear of the hypo-onto-morph. It is thin, long, delicately molded, and the helix is very slightly rolled in, being a mere margin rather than a heavy roll. The distance between the helix and anthelix is great above, and the helix disappears below except for a flat surface with a margin which merges into the lobule that is often absent, the helix then passing diagonally downward directly into the cheek. The concha is long vertically, and its border, the anthelix, projects so much that viewed from behind or in front it seems to be further away from the head than the helix. The tragus and antitragus point outward and often project beyond the helix. Looked at from behind, the rim of the helix presents the shape of the italic letter *f* or the old English letter *ſ*, and seems to have been seized between the thumb and forefinger and twisted upward and backward. The helix is therefore closest to the head at its lower extremity, the lobule, and also at the point where Darwin's tubercle should appear: and it is further away from the head at its summit, also at a point immediately behind the concha. This gives a wavy or spiral effect to the helix, which is very characteristic of this form of ear. The ear is thin and the lines are fine and close together.

The meso-onto-morph ear is somewhat intermediate between the other two forms although it has distinctive characteristics. It is large, heavy-looking and soft, more nearly flat than either of the other forms, and it has a lobule that forms a sloping shelf. The rim of the helix is large, oval and heavy looking. The ear is a large shallow bowl, with sides broad and flat, and a rim heavy but not rolled in very much.

The stability and permanency of the ear form have enabled me to classify types that would otherwise have been almost, if not absolutely, impossible of classification. The form of the face and head are molded by the development of the teeth, the enlargement of the bony sinuses around the nasal chambers, by the action of the muscles of mastication and by the extent of the erectile tissues of the nasal cavities, as well as by the action of the facial muscles through the expression of the emotions; but the ear form is laid down in cartilage, a stable tissue, it is not so prominent as the eyes, nose and mouth, and not so liable to natural and sexual selection, nor is it subject to physiological influences as other features, therefore, it has remained constant in form while other structures have undergone greater variation. The ear form has probably remained constant throughout tens of thousands of years since the three types became fixed, and in the mixtures of the different forms due to interbreeding the ear retains its

original characteristics to a great extent, and is found pure in the greatest variety of peoples in all parts of the world.

In a comparison of the dispensary negro population, or the negro patients of the Touro Free Dispensary, with the general negro population, or the negro people on the streets of New Orleans, it is found that the difference is as follows:

TABLE II.

	Hyper-	Meso-	Hypo-
City Streets	48%	45%	7%
Dispensary	71%	24%	5%

The hyper-onto-morph has a greater morbidity and this is coincident with the great number of the mulatto or light colored element among the negroes.

The hyper-onto-morph among the whites apparently has not a greater morbidity, because the percentages of the three forms on the streets of New Orleans and in the dispensary are practically identical:

TABLE III.

	Hyper-	Meso-	Hypo-
City Streets	80%	18%	2%
Dispensary	80%	19%	1%

The percentages of all forms in the total of the 894 cases utilized in this study are as follows:

TABLE IV.

	Hyper-	Meso-	Hypo-
White	76.6%	21.2%	1.6%
Colored	45.0%	49.0%	6.0%
Total	59.4%	36.3%	4.3%

Further analysis of the colored people given in Table 4 reveals the following figures:

TABLE V.

	Light Colored 39%	Neutral Brown 44%	Sooty Black 17%
Hyper	55%	42%	28%
Meso	39%	51%	64%
Hypo	6%	7%	8%

The significant facts here are that with an increase of pigmentation there is an increase of the hypo- and meso-onto-morph, and with a decrease of pigmentation there is an increase of the hyper-onto-morph. The light colored negroes include several albinos and all the octoroons, quadroons, mulattoes and sambos. The lighter color is due to recent mixtures of negro and white, and the darker colored are of purer African extraction. The indication is that the white is hyper-onto-morph and the negro is meso-onto-morph with some hypo-onto-morph.

Comparing Table 2 with Table 4 a discrepancy in the percentages of dispensary negroes will be noticed. This is due to the fact that negroes of all the clinics, including nervous diseases, eye, ear, nose, throat and genito-urinary diseases are included in Table 2, whereas only medical clinic cases are included in Table 4. The fact that more hyper-onto-morphs are found among the dispensary negroes of Table 2 would indicate that the hyper-onto-morph is more susceptible to nervous diseases, eye, ear, nose, throat and genito-urinary diseases than are the other two forms. This is undoubtedly true and will be demonstrated in part in the subsequent consideration of the diseases in detail.

In any consideration of this study it must be borne in mind that the personal equation is to be considered. A diagnosis is often overlooked because it is not looked for, but where the diagnosis is given it is self-sufficient evidence. The omission of a diagnosis cannot well apply to tuberculosis, however, because I was on the lookout for this disease in an effort to determine exactly, if possible, the physical type with which it is associated. Observations in the Philippines had convinced me that the disease is especially virulent among the hyper-onto-morphs. This has been confirmed both among the whites and among the colored people of New Orleans. Whatever else may be the result of this investigation the most emphatic substantiation of previous observations is here presented. If other facts are significant they stand for themselves, no effort has been made to prove or disprove them.

Each disease will be discussed here in turn, in relation to the three physical forms previously described.

PULMONARY TUBERCULOSIS.

One hundred per cent more white than colored persons came to the Touro Dispensary afflicted with pulmonary tuberculosis among the 894 individuals examined, but this may be of no great significance, only the chance distribution in a random sample of the city sick; another thousand individuals might show a different proportion altogether. Neither does the one hundred per cent excess of males of both races who have tuberculosis, present any great significance, although both proportions are true and either may be significant. White people may be more susceptible to tuberculosis than colored people, and males may be more susceptible to tuberculosis than females, but this can be determined only by many thousands of records from all parts of the world and under all conditions of life.

When, however, practically every individual who is afflicted with tuberculosis, white or colored, male or female, is of one type, a type more distinct than any other human type, readily separable from the other types by differences in ear form, physiognomy and the length relations of body parts, then one comes to realize that less than a thousand individuals taken as a random sample of the city sick is sufficient to determine the susceptibility of such a type to tuberculosis. This type is the hyper-onto-morph, the slender individual, with long head, face, nose and extremities, and ear with everted tragus, and antitragus, and anthelix, and with rolled out helix. Only two individuals of the 134 afflicted with tuberculosis had no trace of the hyper-onto-morph form. No. 8797, white male, age 55, a modified meso-onto-morph with kyphosis, bronchitis and acute indigestion, and No. 47, white female, age 47, a modified meso-onto-morph with sacro-iliac subluxation. The remainder of those who have pulmonary tuberculosis are pure or mixed hyper-onto-morphs. In confirmation of this I have

records of 38 post mortem examinations of individuals found to have tuberculosis, of whom there are 11 white hyper-onto-morphs, 23 colored hyper-onto-morphs, 4 colored meso-onto-morphs, and 1 colored hypo-onto-morph. It cannot be said that no other form except the hyper-onto-morph will have tuberculosis, nor can it be said that all hyper-onto-morphs will have tuberculosis, but it can be said that the hyper-onto-morph is susceptible to tuberculosis. Small, slender, hyper-onto-morphs with small, round, everted ears were found with tuberculosis most frequently. Tall, slender, hyper-onto-morphs with everted ears that have no lobule are also susceptible and often have the most aggravated type, cavity formation with bronchiectasis.

Blondes as well as brunettes of the hyper-onto-morph form have the disease, but very few blondes are recorded, probably because of the preponderance of brunettes in New Orleans. There were a few cases like the following, however:

White German-American, blonde, male, age 23. Cough and expectoration for two months. Pharyngitis, laryngitis and signs of incipient pulmonary tuberculosis.

White, blonde, female, married, age 30. Hacking cough for one year, hoarse at times, and free expectoration. Has lost 30 pounds weight in the past 18 months. Dullness at the left apex with bronchial breathing and subcrepitant râles over this area.

The form of hyper-onto-morph that is believed to represent the primordial or original prehistoric type of hyper-onto-morph, is susceptible to tuberculosis but is very resistant to a fatal issue with the disease. This form of hyper-onto-morph is similar to the early cave man of Europe known as the Cro-Magnon race, and is intermediate between the Mediterranean form of the hyper-onto-morph, and the meso-onto-morph. This Cro-Magnon form of the hyper-onto-morph is tall, raw-boned, with large face—long and wide—prominent cheek bones and large nose and long everted ears with pendant lobules, and is distinctly different from the Mediterranean form of the hyper-onto-morph who is small, slender, thin, dark, with small face, long, thin nose and face, and ears of the everted form, although they are both similar especially in ear form. The Mediterranean race has been derived from forms similar to the Cro-Magnon race through life in cities, tropics, semitropics, etc., and may be only the attenuated form as a result of deficient nutrition, etc., incident to this life. The early form of hyper-onto-morph (Cro-Magnon) is at present more resistant to tuberculosis than the derived form (Mediterranean). A few illustrations will suffice.

No. 2287. White male, age 55. Hyper-onto-morph (Cro-Magnon). History of tuberculosis for 20 years, beginning with spitting of blood. At present emaciated, emphysematous, with pigeon-breast. Dullness over left infraclavicular region 4½ x 8¾ inches in area. Dullness at both apices and to angle of scapulæ behind. Râles below scapulæ. Temperature 97° to 99.5° F. Lost 2 lbs. in 3 years. Progress favorable.

No. 6487. White male, age 64. Hyper-onto-morph (Cro-Magnon). Was treated for pulmonary and laryngeal tuberculosis in the Touro Dispensary in 1907. Condition at present: Fair nutrition, process in lungs still limited to right apex. Dullness, bronchial breathing, squeaks in supraclavicular region. Few subcrepitant râles in infraclavicular region. Larynx shows no signs except slight roughening of plicæ interarytenoideæ.

No. 6616. White female, age 61. Hyper-onto-morph (Cro-Magnon). Was tested for pulmonary tuberculosis in Touro Dispensary in 1908. At present emaciated. Kyphosis. Scoliosis. Both apices involved. Temperature 99.3° F.

No. 6980. Colored (sooty black) male, aged 52. Hyper-onto-morph (Cro-Magnon). Four months previous had had one rib broken and two "strained." Spat blood for two days. Has since lost about 20 lbs. in weight. At present there is dullness at left apex posteriorly, with increased vocal fremitus over this area.

No. 7061. Mixed Negro-Indian female, age 57. Hyper-onto-morph (Cro-Magnon). History of fever, heavy cold, profuse expectoration, loss of weight, no appetite, bowels costive. At present emaciated, a few scattered râles over left side, where there is a peculiar grating sound with râles intensified over the 3d rib. Tubercle bacilli are present in the sputum.

No. 103. Benito, male Chinaman, age 88. Hyper-onto-morph (Cro-Magnon). Charity Hospital. Pulmonary tuberculosis.

These examples will suffice to show that the types are not racial but anatomical, and that the individuals attain an advanced age in spite of the tuberculosis.

There can be no doubt that the hyper-onto-morph of all kinds is susceptible to tuberculosis, and although the tendency may be aggravated by unhygienic conditions, it is largely responsible for the prevalence of the disease.

Diseases of the Nervous System.

The diseases of the nervous system may be enumerated as follows: Neurasthenia 33 cases, paralysis (all kinds) 18, exopthalmic goitre 12, insanity 6, epilepsy 5, pellagra 5, tabes dorsalis 2, angioneurotic edema 2, sclerosis 1, herpes zoster 1, hysteria 1, torticollis 1, 87 in all. Of these 79 are hyper-onto-morphs, 6 are meso-onto-morphs and 1 a hypo-onto-morph, the last the individual with multiple sclerosis. Of the 6 meso-onto-morphs 2 have epilepsy, 1 paralysis, 1 pellagra, 1 hysteria and 1 neurasthenia. Notable is the fact that all the insane and those with exophthalmic goitre are hyper-onto-morphs.

There can be no doubt that the hyper-onto-morph is susceptible to diseases of the central nervous system.

Diseases of the Alimentary Canal.

The diseases of the alimentary canal are the following: Constipation 161 cases, stomach 14, diarrhœa 6, typhoid fever 5, intestinal parasites 4, and appendicitis 2, 192 in all. Constipation cannot be said to have an affinity for any one form because 49 cases are meso-onto-morphs, 39 hyper-onto-morphs and 1 hypo-onto-morph, the remainder being mixed, 60 of the hyper-meso form and 13 of the hypo-meso form. The forms that have other alimentary troubles are 30 hyper-onto-morphs and 1 meso-onto-morph. Of stomach troubles 9 are simple such as gastritis, 4 are carcinoma, and 1 gastritic ulcer. All are hyper-onto-morphs. Post mortem examination of 3 individuals, dying of carcinoma, of the hyper-onto-morph class was made. Except for constipation, gastro-intestinal diseases pertain to the hyper-onto-morph. There are only 31 cases, however, which is a small number for generalization, but the indi-

cation is that the hyper-onto-morph is susceptible to diseases of the alimentary canal, although this is not so emphatic as for tuberculosis and the nervous system.

Cardiac and Renal Diseases.

Affections under this head include those of the heart, circulatory system and kidneys, arterio-sclerosis and aneurysm. Affections of the heart and kidneys are grouped as one complex but arterio-sclerosis and aneurysm will be discussed separately.

Ninety-two individuals were diagnosed with heart or kidney troubles, and of these 80 are meso-onto-morphs, 11 are hyper-onto-morphs and 1 is a hypo-onto-morph. As will be noticed only 12 individuals had no indication of the meso-onto-morph form. Three of the hyper-onto-morphs have tuberculosis associated with the cardiac or renal condition and 4 are advanced in age. The inference is that the meso-onto-morph is most susceptible to cardiac and renal affections.

Arterio-sclerosis claims 24 meso-onto-morphs, 11 hyper-onto-morphs and no hypo-onto-morph, although 3 meso-onto-morphs have traces of hypo-morphism. The majority of the hyper-onto-morphs are well advanced in age, beyond 50 years, and this may account for the great proportion of them with arterio-sclerosis. The meso-onto-morph is most susceptible to this disease.

Fifteen meso-onto-morphs have aneurysm, only two hyper-onto-morphs (modified) and none of the pure hypo-onto-morphs have this affection, although 6 of the meso-onto-morphs have some hypo-morphism. Aneurysm, therefore, seems to strike the meso- and hypo-onto-morphs.

Post mortem examination of 17 individuals with cardiac or renal troubles gives 15 meso-onto-morphs and two modified hyper-onto-morphs. Seven other individuals with extremely dilated aorta are meso-onto-morphs. There can be no doubt of the association of heart and arterial affections with the meso-onto-morph and the kidney affections may be incidental to these.

Emphysema, Asthma and Pleurisy.

Contrasts and parallels enter here. Emphysema affected 12 hyper-onto-morphs and 4 meso-onto-morphs. Pleurisy attacked the same, whereas asthma attacked 6 meso-onto-morphs and two hyper-onto-morphs. Emphysema affected 12 white persons and 4 negroes, whereas the other two attacked 16 negroes and 7 white persons. The numbers are too few for generalizations yet they are suggestive. The negro may be susceptible to pleurisy yet the form of the negro most susceptible is the hyper-onto-morph. The negro likewise may be susceptible to asthma, yet the form of the negro most susceptible is the meso-onto-morph. The white people may be susceptible to emphysema, yet the form most susceptible is the hyper-onto-morph. That the meso-onto-morph appears to be susceptible to asthma may throw light on the nature of the disease. The indication is that its muscular nature is paramount. Post mortem examination of 19 subjects with pleural affections reveals 11 hyper-onto-morphs, 7 meso-onto-morphs and 1 hypo-onto-morph.

Arthritis.

Arthritis deformans claims 13 hyper-onto-morphs and 2 meso-onto-morphs; simple arthritis claims 12 hyper-onto-morphs and 2 meso-onto-morphs, one of which is mixed with hypo-onto-morph, therefore a greater tendency to arthritis on the part of the hyper-onto-morphs is evident.

Anemia.

Every anemic individual observed is a hyper-onto-morph, 14 in all, including 1 with pernicious anemia.

Eye Troubles.

Every individual with affections of the eye is a hyper-onto-morph, 5 of whom are white and 5 colored.

Venereal Diseases.

The relative proportion of the different forms infected with venereal disease is almost exactly the same as the relative number of the different forms in the total number examined, therefore no inferences may be drawn. There seems to be, however, a greater tendency on the part of the hyper-onto-morph to syphilis. There are 31 hyper-onto-morphs to 14 meso-onto-morphs with syphilis, whereas there are 24 hyper-onto-morphs to 17 meso-onto-morphs with other affections of the genito-urinary apparatus.

Traumatic.

Accident cases include a large number of sacro-iliac subluxations, of which all among the white people are hyper-onto-morphs, whereas 11 of the 13 among the colored people are meso-onto-morphs. This is another way of saying that the white people are hyper-phylo-morphs and the colored people are meso-phylo-morphs to a large extent. Other accident cases are distributed among the three forms in about the normal proportion.

Acute Infectious Diseases.

These include the following cases not before given:

Bronchitis 14, malaria 10, rheumatism 6, tonsilitis 10, coryza 6, jaundice 5, measles 3, mumps 2, cystitis 3, boils 1, endocarditis 1, pneumonia 1, influenza 1, septicemia 1, sore throat 1, 64 in all, of which 36 are hyper-onto-morphs, 23 meso-onto-morphs and 5 hypo-onto-morphs. The last is a higher proportion than normal, the other two have about the usual proportion. It may be that the hypo-onto-morph is susceptible to acute infections, but this is only suggested, not proved.

The other diseases are so few in number and so diverse in form that deductions would be unfair.

Inferences.

The present study has demonstrated that morphologic entities which may be called character-complexes may be distinguished by their ear form, physiognomy and body parts. Three definite forms may be segregated from any group of

people, and these three forms I have designated hypo-onto-morph, meso-onto-morph and hyper-onto-morph, depending upon their apparent position in the scale of evolution or development—their ontogenic position.

The hypo-onto-morph may be susceptible to acute infectious diseases and cardio-renal affections, but their number is too few for final judgment.

The meso-onto-morph is susceptible to disease of the tissues derived from mesothelium, especially to diseases of the circulatory system and kidneys.

The hyper-onto-morph is susceptible to diseases of the tissues derived from epithelium, especially to pulmonary tuberculosis and diseases of the alimentary canal and central nervous system.

THE LAST ILLNESS OF LOUIS XIV.*

By Carroll E. Edson, M. D., Denver, Colorado.

The deaths of kings who die in their beds are usually recorded by the bare statement of the date, and the historian passes on to expound his theory of the political significance of the reign just closed. The human side—the sickness, the suffering and the dying of a man—which the physician sees, is rarely told, and we are often ignorant of the cause of death.

The last days of Louis XIV have been described with great precision by several memorialists who were witnesses of the events; Saint Simon, Dangeau, and Anthoine, who was his *valet de chambre,* have all left accounts, and the recent biography of Georges Maréchal, who was the first surgeon to the Grand Monarch, has supplied further most interesting details of the illness. I have thought that an account of it might be worth your listening to; for it will tell not only the story of the pathology of the King's death, but between the lines give some interesting glimpses of the state of things medical in the year 1715.

First, a few words of introduction. The last two years of the King's life had been full of trial and disappointment—official and personal sorrows. The Treaties of Utrecht and Rastadt (April, 1713 and March, 1714) had brought to a close the long and exhausting war of the Spanish Succession, and with it put an end to the great ambitions of the King for an extended family dynasty. The failure of his arms and plans were heavy disappointments. At home he had the sorrow of seeing the direct line all but wiped out by death. His only son, Monseigneur, had died in 1711 (April 14), leaving as dauphin the Duke of Burgundy. In 1712 the Duchess of Burgundy, a great favorite of the King, died suddenly on February 11. The Duke died with equal suddenness on the 18th, and their son, the little dauphin, Duke of Brittany, followed them to the grave on March 9th, leaving as direct heir to the throne the Duke of Anjou, great-grandson to Louis, a delicate child of two years.

A year later, on May 4, 1714, the Duke of Berry, the remaining grandson, died. This brought the throne but one life away from the Duke of Orleans, the King's nephew, whom he cordially disliked. To these tribulations of France and family were added the trials of conscience over the Bull Unigenitus of Clement XI and the Jansenist opposition. So much did Louis worry over this matter, that in March, 1714, M. Fagon, the first physician, advised the King that he ought to quiet himself in the matter of this constitution, if he did not wish to impair seriously his health. But the pressure of Madame de Maintenon and the Jesuit party prevented any compromise, and the Cardinal Noailles, Archbishop of Paris, and the fifteen Jansenist bishops remained unreconciled to the time of the King's death.

To all these anxieties was added that of the financial exhaustion of the realm and the problem of raising revenue from a diminishing and starving population, to maintain the extravagance of the court at Versailles. "The whole nation was starved and became dreadfully thin; from this time onward for a century the caricaturist draws the Frenchman as a thin, tall, lantern-jawed creature." "Starved skeletons clamored round the gates of Versailles, and could hardly be kept out of the royal presence." The King had always a very robust appetite, and, while the population starved, ate so much that the courtiers were alarmed. When we bear in mind that all these cares were laid on the shoulders of an old man of over seventy-six (he was born in 1638, and had reigned since 1643), we can the more readily appreciate the reason for his illness.

For over a year the King's health had been gradually failing. His household valets had noticed it, and watched the decline without daring to say a word. Fagon, the first physician, himself much broken in body and mind, was of all the household the only one who noticed nothing. Maréchal, the first surgeon, spoke of it to him several times, but was always curtly rebuffed. By spring the King's feebleness was so marked—and a rumor that his legs were swollen being confirmed by the British Ambassador, who peeked under the table to see—that wagers on his health were laid in the clubs of London. Learning of these wagers, the King tried to conceal the uneasiness they caused him, and on June 12 (1715), moved to Marly, his favorite residence, about four miles from Versailles. Here he devoted himself assiduously to his usual diversions of walking, hunting and holding military reviews. Just before the King's departure, Maréchal, who had in vain tried to arouse Fagon to an appreciation of the King's condition, felt it his duty to warn Madame de Maintenon of her husband's danger. Going one morning to her apartments, he told her what he foresaw, and how grossly Fagon was deceived. He assured her that the King, whose pulse he had frequently felt, had for some time been running

* Read at a meeting of the Denver Medical History Club.

a little fever; that his constitution was so good that with proper care there was still plenty of room for recovery; but that if the illness were allowed to gain headway there would not be. Madame de Maintenon was much provoked, and all Mareschal got for his zeal was a storm. She told him that it was only personal enemies of Fagon who disputed his opinion of the King's health, and that the ability, watchfulness and experience of the first physician put him above any mistake. So Mareschal learned, as have others, that it is folly to discuss her physician with a woman, and affairs went on in the old way of high living, heavy eating and extravagance, until the fatal illness came upon the King.

From early in July Louis had fixed upon August 10 for leaving Marly; but on that morning he was indisposed, and said to Mareschal that he felt greatly confused, and thought a bleeding would help him. All his life he had been accustomed to frequent venesections. Fagon, however, ruled the proceeding unnecessary, and the King returned that evening to Versailles. The next day the confusion continued, and on the following morning he felt a severe pain in his left leg. Fagon attributed it to an attack of sciatic gout, and paid no attention to it other than to give the King a purge. By night, however, the King was worse, and as the first physician prescribed no new remedy, Blouin, the King's first valet, who was devoted to him, insisted that a consultation be called between the physicians of the court and those of Paris. He only expressed the general opinion; for at the same time Marshal de Villeroy wrote to Madame de Maintenon: "You are with the King, Madame; you see him, and you know his condition. I have nothing to tell you or to suggest, save this: Are you willing that the opinion of Fagon alone shall decide the King's life? The lowliest villager, when his family think him in danger, gathers the ablest doctors he can afford for consultation. Shall the King be the only one in his realm deprived of such help? Can M. Fagon wish to decide so important a matter alone? In truth, Madame, it makes one shudder. All think as I do, but dare not say it."

At first Fagon made objections; but reflecting on the tremendous responsibility he assumed, gave in, and four of the leading physicians of Paris were summoned for the next day.

In spite of the pain of his supposed sciatica, the King, after mass, held a public reception, giving audience to the Persian Ambassador, and remained standing throughout the ceremony. We are reminded of King Edward VII holding the privy council the first day of his last illness.

At six that evening, while going to Madame de Maintenon's apartments, which were located near his on the first story of the chateau, the King was taken with such severe pain in his leg that he could scarcely walk the few steps necessary. Within an hour the pain had increased so that it was necessary to send for Mareschal, the first surgeon. He examined the leg in company with Fagon. They found only a little redness just below the garter. Mareschal rubbed the leg with hot cloths, which gave a little relief to the pain, and the King was able to go back to his room. About eleven o'clock the same pain returned so severely that it was decided that Fagon should stay by the bedside that night with M. de Chancenetz, the first gentleman-of-the-chamber in residence, whose duty it was, while the physician-in-ordinary, Boudin, the first surgeon, Mareschal, and the apothecary, Biet, lay down in the large counsel chamber adjoining with the valets Anthoine and Bazire. Mareschal was called on many times in the night to rub the King's leg; but it gave only short respites from the pain.

The next morning, August 14, the physicians summoned by Fagon from Paris arrived at Versailles. The names of two have come down—Helvetius and Falconet. After feeling the King's pulse, they retired to the councilroom for consultation. Anthoine in his journal wrote: "One never saw better the small resource there is in medicine, for after a long debate they decided that the King should be given some asses' milk, and a few hours later a second consultation determined them to suspend the decision reached at the first in as much as the pain had increased after noon." At the first of the 18th century asses' milk was considered a very efficient remedy. As De Bieire says, "It had the advantage over the specifics of that absurd medical epoch of being harmless."

On the 15th the King had less pain, and there was hope of a speedy recovery, but he still had great difficulty in moving.

The morning of the 16th, after a profuse night sweat, he could hardly be lifted from the bed to an armchair for his valets to dry him and change his linen, so much did the least movement increase his pain. From this day on, so long as he was able to leave his bed, it was Mareschal, his surgeon, and the Marquis de Chancenetz who carried him to his armchair.

On the 17th, however, the King got into a wheel-chair, and went to Madame de Maintenon's. In the evening the pain increased, and Mareschal was called to dress a sore on the leg, which, till then, had been thought unimportant. To the first surgeon the diagnosis of gangrene was manifest; but he held his tongue that night, and Fagon talked of sending for some Bourbonne water, and declared there was no fever.

Thus the first physician persisted in his lack of insight. His opinion no longer deceived any one, "for the condition of the King" writes Saint Simon, "of whom I have more accurate news from Mareschal, shows clearly that he can last but a few days."

On the 19th the nature of the King's illness was only too sure. When the doctors came at two o'clock to see the leg dressed, they found a great change. It was badly swollen and there was a black area on the instep.

From this time Fagon appeared to be uneasy. On the 20th he ordered the leg kept for an hour in a bath of spiced Burgundy wine; but Mareschal's frictions were the only things which gave any relief. The bath had no effect. Fagon now proposed, himself, a second consultation, and the physicians were again summoned from Paris on the 21st. "They felt his pulse in order of seniority," says Anthoine, "and appeared satisfied to find less fever." In spite of this optimism, the King grew worse toward night. Mareschal came to dress and rub the leg, as he did almost every hour. He found the process greatly extending, and told Fagon, who

proposed to the King to have the physicians out from Paris again. To ask almost daily consultations, after obstinately attempting single-handed the care of the King, showed that Fagon at last appreciated the soundness of Mareschal's repeated advice.

Four other physicians were called in the next day, August 22, among them Dodart and Dumoulin. At the close of their consultation they prescribed quinine and more asses' milk.

On the 23d they returned, eager to verify the improvement brought about by their desperate remedy. Mareschal unbandaged His Majesty's leg in the presence of the physicians, who did not dare show their surprise at finding it in so bad a condition, and laid the blame on the poor female ass. They made several visits during the afternoon. The King was very restless, and Mareschal was kept busy unbandaging the leg, rubbing it, and rebandaging it.

On the 24th Fagon called another general consultation of all the physicians of the court, and all those of Paris who were at Versailles. They came in full ceremony, felt the King's pulse, and ordered the leg wrapped in cloths soaked in camphorated brandy. In the evening the leg was quite black to the foot.

The condition being thus clearly surgical, and Mareschal's opinion the official one, he could speak to the first physician with the certainty of being listened to. He profited by it to do several of the Masters of the Surgeon's Guild the honor of calling them in consultation over the King, as Fagon had done the physicians. The first surgeons called in were Ledran, Arnault, Gervais, Dionis and Petit, with some others of the more renowned.

Up to this time the King, in spite of his suffering, had not ceased for a single day to attend to the affairs of state and to receive his ministers. Changing his routine as little as possible, he had forced himself to dine in public, a long and tedious ceremonial, and to pass the evening in his study with the princesses. But from the 24th of August he never left his room.

In the afternoon of the 25th the surgeons, Masters of St. Côme, arrived at Versailles at two o'clock, and inspected the King's leg in the presence of the court surgeon and physicians. They looked at each other and silently shook their heads. Their faces showed the hopelessness of cure. At their consultation they decided to make a few small incisions in the leg to give outlet to the pus. This operation was put over till the next day, however.

A few hours after the surgeons' departure the King had a fainting spell, and realizing the gravity of his condition, gave no further thought to concealing it. He asked for extreme unction, and received the sacrament piously; then, having given audience to his ministers, he said an affectionate word to each of the princes.

On the 26th about ten o'clock the surgeons returned to see the incisions made in the leg. Mareschal did the operation in presence of the other surgeons and physicians; but, although he made deep cuts, His Majesty felt nothing, till going each time higher and deeper, at last the King cried "Oh, Mareschal, you hurt badly."

Several different accounts are given of this proceeding, all written more or less with courtly flattery. I shall not recount them, as they have too much the color of fiction, and no bearing upon the medical narrative. One, however, seems fairly authentic, at least in its essentials. At the close of the operation the King said to Mareschal, whom he had always been fond of and implicitly trusted: "I see there is no cure. Be frank with me. How long have I to live?" "Sire," said Mareschal, "we may hope until Wednesday." "My warrant for Wednesday, then. I will be ready," said the King. At once he began making his final arrangements. About noon he had the Duchess of Ventadour bring him the little dauphin, to whom he counselled moderation and the duty of solacing his people. "You are soon to be King of a great realm. What I commend most earnestly to you is never to forget the obligations you owe to God; remember that you owe all you are to Him. Try to keep peace with your neighbors; I have been too fond of war; do not imitate me in that, nor in my too great expenditure." Then calling the Duke of Orleans, the regent-to-be, he arranged with him the measures to be taken on his death, adding, "You are now fortunate, for you have one King in the tomb and the other in the cradle." As Kitchin says, it was a courteous and pleasant manner of parting with a kinsman whom he had never liked or trusted. At half-past twelve he heard mass in his chamber, and after an interview with Cardinals de Bissy and de Rohan, sent a message of good will to Cardinal Noailles. He then called to his bedside the officers who were in the apartments, and bade them a gracious adieu, after which he had the princesses of the royal family come in. They had been waiting in the adjoining robing-room, and entered in the manner then considered most becoming such an occasion, wailing and crying at the tops of their voices. "Though they were allowed in but a moment," writes Dangeau, "I do not see how the King endured it." In spite of the fatigue of the day, which we must admit was a pretty busy one for an old man with senile gangrene, the King picked up a bit toward night; and when Mareschal dressed the leg, he found the gangrene had not extended.

The next day, the 27th, the patient was about the same. He passed the day with his confessor, the Jesuit, Le Tellier, and Madame de Maintenon.

On the 28th he was so weak that they thought him dying; but he rallied and said to his sobbing attendants, "Why do you weep? Did you think I was immortal?"

About eleven o'clock a doctor from Marseilles arrived at the chateau, claiming to have a sovereign remedy against gangrene, and pretending to be a doctor of the Faculty of Leipzig. Then, as now, the surest and newest pharmaceutics seemed to be "made in Germany." The man had been sent from Madame de Maintenon to Père Le Tellier, and from him to Fagon, who had passed him on to Cardinal de Rohan, and then to Mareschal. Everywhere he was turned down as a quack, a sorcerer or a fool. Mareschal, who was always

courteous, asked the German what he hoped to do, knowing the King could live but a day. "I have two elixirs," he said, "one will give the King some appetite, for he has taken no food for a week. The other will at least retard the progress of the gangrene, if it does not stop it." "I have not faith in what you say," said Maresehal, "but there is no harm in trying everything." Who of us has not consented to such nostrum administration under similar conditions of family distress.

Fagon, staunch old regular, tried to oppose the trial of this empiric, at which the charlatan abused him so roundly and brutally that the old physician, who was accustomed to do the bullying himself and to be respected even to trembling, was much abashed, and retired. With the consent of the Regent, the quack, who called himself Dr. Lebrun, gave the King ten drops of his elixir in three teaspoonfuls of Alicante wine. The drug was said to have been made from the carcass of an animal in the same way that English drops were made from the skulls of men.

During the 17th and well into the 18th century, *liquor cranii humani* was a highly prized remedy, prepared from unburied skulls, those of criminals by preference. On this point all authorities were agreed: that the remedy was of little use unless prepared from the skull of a young man who had died a violent death. In London the druggists sold skulls on which was grown a little green moss, like that on oak trees. Pomet in 1694 wrote, "These skulls mostly come from Ireland, where they let the bodies of criminals hang on the gibbet-tree till they fall to pieces." The market price varied from eight to eleven shillings, according to the size and the growth of moss. Germany was the principal purchaser. During the last illness of Charles II of England, who died from a stroke of apoplexy, one of the remedies used was twenty-five drops of the spirit of human skulls.

The charlatan's dose revived the King for a few hours, and fickle court rumor spoke of a cure; but the impostor had not as yet been shown the leg, and his assurance wilted when he saw it gangrenous to the knee.

The day of the 29th, during which the King took several doses of the elixir, was fairly comfortable. In the evening he was able to eat two biscuits soaked in wine—the first food in several days. At half-past ten, when Mareschal dressed the leg, the gangrene had extended above the knee, and the thigh was much swollen.

During the morning of the 30th, the King was in an almost continuous state of collapse, and Lebrun left, saying he had come too late. The faithful Mareschal did not leave the bedside, and several times was on the point of calling the priest. No one was in the room save the most necessary attendants, Madame de Maintenon and Mareschal. About five o'clock, the King being unconscious, Madame de Maintenon, who, it must be remembered was eighty years old, left the chateau and went to St. Cyr.

There was no change on the 31st: the King was unconscious all day, only his great vitality holding death at bay. In the afternoon the Duchess of Maine (wife of the King's bastard by Madame de Montespan), insisted on giving the King a remedy devised by the Abbé Aignan for small-pox. No opposition was made. At ten o'clock the prayers for the dying were repeated. The King appeared to rouse a little, and to repeat mechanically the responses, and again became unconscious.

About five o'clock in the morning, Sunday, September 1, the King lost absolutely every sign of life save respiration. Mareschal uncovered the leg in presence of the medical staff and several distinguished courtiers. The whole leg and thigh was gangrenous, and the process had extended up on to the trunk. Two hours later the agony began, and lasted until quarter of nine, when it ceased with a few sighs and two tracheal gasps, without any convulsion. Louis XIV was dead.

While the Duke of Orleans and the princes went to salute the little dauphin as King, George Mareschal with the help of the chamber-boys took the body from the bed, changed the linen, and replaced it in a sitting posture in the same bed. He placed a crucifix in the hand, and to keep the mouth closed tied a bandage under the chin, pinning it on each side to the night-cap. It was in this position that the Court was admitted to view the body in the afternoon.

The next day, September 2, the autopsy was made. It had long been the custom to examine the bodies of all members of the royal family after death. It was this routine examination which enabled Mareschal to disprove the unpleasant rumors of poisoning when the family of the Duke of Burgundy died in such rapid succession. The proceeding was one of great ceremony, and known officially as "The Opening." The officers of the chamber and of the wardrobe carried the King's body into the great antechamber of the royal apartments, and placed it on a table—probably that at which the King was accustomed to dine in state. The Regent designated the Duke d'Elbeuf and Marshal Montesquion to preside at the ceremony. The Duke of Tresmes, first gentleman of the bedchamber, and the Marquis Maillebois, master of the wardrobe, were present ex-officio. The first physician, Fagon, took his position near the body, having behind him in addition to the medical household of the King, two doctors from the Faculty of Paris, deputed by the Dean according to custom. When all the spectators were in place, the first surgeon and the first surgeon in succession, George Mareschal and his son Louis, with the help of their assistants and two Masters of the Guild of St. Côme, delegated by custom, divested the royal body of its robes of state and covered it with a sheet, which wholly concealed it. Then George Mareschal fulfilled the last duty of his office, and in person began the autopsy. He folded back the cloth from the head, and sawing the skull, exposed the brain. Placing a napkin at once over the part examined, he opened the thorax and removed the organs. Again covering the chest, he passed to the belly, taking out the intestines and measuring their length. After this he laid open the leg its entire length. As the first surgeon dissected each part or organ, the first physician dictated the formal notes to be recorded in the report. Amid these solemn surroundings Fagon once more asserted the predominance of

medicine over surgery. The autopsy over, the physicians drew up their report, which reads:

September 2d, 1715, the body of the King, Louis XIV, surnamed the Great, because of his rare virtues, was opened by M. Mareschal, first surgeon of the King, in the presence of His Majesty's physicians and surgeons and other persons appointed by the Duke of Orleans to be present.

The exterior of the left side was found gangrenous from the extremity of the foot to the top of the head; the skin peeling everywhere, but less on the right than on the left; the body extremely distended and bloated; the bowels much altered with inflammation, especially those on the left side; the large intestines extraordinarily dilated. The kidneys were fairly normal and natural; but in the left one was found a small stone similar to those the King had several times passed without pain while in health. The liver, spleen and stomach were in a normal condition, both externally and internally. The lungs, as well as the chest, normal; the heart in very good condition, of ordinary size; the terminals of the great vessels ossified. All the muscles of the throat gangrenous. On opening the head, the dura mater was found adherent to the cranium, and the pia mater marked with black areas along the falx; the brain sound, in natural condition, outside and within. The interior of the left thigh, where the King's disease began was completely gangrenous in every part; all the blood in all the vessels totally disorganized, and very scanty in amount.

Done at Versailles this second day of September, 1715.

The autopsy finding of the exceedingly dilated colon is of great interest, and explains to us, if it did not to his physicians, much of Louis XIV's medical history. All his life he was accustomed to take regularly rather drastic purges, and for years had frequent recourse to high enemata. Indeed it was the Grand Monarch who made the enema truly fashionable in Europe. The journal of the King's health, kept by the first physician, shows that between 1647 and 1715 the King took by reason of need or precaution between 1500 and 2000 purgative doses—and purges in those days were not candy cathartics. In addition there is a record of many hundred enemata. We can well understand the need.

Mareschal allowed all the physicians present at the ceremony to sign before doing so himself; but protested against this subordination of the first surgeon to the ordinary physicians. In 1748 one of his successors, M. de la Martinière, performed an autopsy on the *petite* Madame, daughter of the dauphin, refused to sign the report, claiming that his name should follow immediately that of the first physician.

After signing the report the physicians withdrew, leaving Mareschal to embalm the body. The first apothecary had prepared a powder of twenty-six aromatic drugs, and another into which entered twelve kinds of odorous gums. He brought in also a jar containing a mixture of oil of laurel, liquid styrax and balsam of copaiba.

Mareschal filled the King's heart with the balsam powder, placed the organ in a lead box, which he enclosed in a casket of sandal-wood, which in turn was sealed in a silver reliquary. Then he put the royal entrails—not only the intestines, but all the viscera removed at the autopsy—into a similar series of three cases. Layers of aromatic powder separated each organ from the adjoining ones.

By the King's wish the first reliquary was to be taken to the chapel of the Jesuits in the Rue St. Antoine; the second to Nôtre Dame.

The Duke of Tresmes then held the King's head, as custom dictated, while Mareschal stuffed it with powders and gums. He did the same with the body, and opening the four limbs filled them with the same mixtures. Then with a brush he smeared the whole body with the balsam prepared by the apothecary. Wrapping the head, the limbs and the trunk with linen bandages, he placed the body on a large, waxed sheet, which he bound stoutly about it, "as one would do up a package to go by express." (Literally: stagecoach.) Having put a shroud on the corpse, his duty was done. The Duke of Tresmes and the Marquis of Maillebois, gentlemen of the bedchamber, placed the body in a double casket.

After the body was taken to its last resting place at Saint Denis, the King's detractors in allusion to Mareschal's preparations, published a pasquinade.

À Saint Denis comme à Versailles
Il est sans coeur et sans entrailles.
Now at St. Denis as at Versailles
He has no heart and no entrails.

But far from partaking in this untimely joy, the first surgeon of Louis XIV said with the officers of the court, "We have lost a great King and a good Master."

If I have not already tired you with this rather long account of a simple case of senile gangrene occurring in the course of a general arterial sclerosis brought on, doubtless, by the many years of gross overeating and imperfect colonic elimination, you may be interested in knowing a little about the two principal attendants of the King, his first physician and first surgeon, whose portraits I am able to show you.

Guy Crescent Fagon, the first physician, was born in Paris, May 11, 1638, of noble blood. His mother was niece of Guy de la Brosse, founder of the Royal Botanic Gardens. He received his M. D. degree from the University of Paris, and took for his thesis the circulation of the blood, maintaining Harvey's new theory somewhat to his disadvantage. He was made botanist to the King, and travelled extensively in Auvergne, Languedoc, Provence, the Alps and the Pyrenees at his own expense. He was later Professor of Botany and Chemistry at the Jardin des Plantes, and director of the Gardens. He was editor of the Hortus Regius, 1665. In 1677 he was chosen by Mme. de Searron as physician to the King's bastards; later she obtained for him the appointment as physician to the Queen, and on the death of Maria Theresa in 1683, the post of first physician to the royal children. In 1693, as Madame de Maintenon, she secured his appointment as first physician to the King, a most important and lucrative position. While you are looking at this picture of the man, I will read the description which the Princess Palatine wrote: "Of Doctor Fagon's appearance you can hardly form an idea. He has thighs as slim as a bird's legs; a mouth filled with teeth which are all yellow and slimy; projecting big lips which give him a protruding mouth; drooping eyes; a decidedly yellow complexion; a narrow face, and an air as evil as he is in reality." This is the pen sketch of a woman who did

GEORGES MARESCHAL,
Seigneur de Biévre,
Chevalier de l'Ordre de Saint-Michel,
Premier-Chirurgien de Louis XIV et de Louis XV.
1658–1736.

GUY CRESCENT FAGON.
1er Medecin du Roy.
Né à Paris le 11. May 1638. Mort le 11. Mars 1718.

not like the man; for he had many enemies, as one in his position must. Another satire on him ran:

> He lives only by his regimen,
> Skinny, bow-backed, hideous;
> He shambles like a quadruped;
> From his figure you'd take him for a Zed.
> A forest of black hair surrounds
> His tousled head and face.
> He terrifies the populace;
> For all who see him think at first
> They look on death's own skeleton.

Hated by some, feared by all, he was still loved by many, and must have been a man of no little character and force; for he was held in high regard by the Ministers, and filled for over twenty years his responsible position, to the entire satisfaction and confidence of an exacting monarch in an intriguing court.

Though the physician to a most robust and gormandizing King, Fagon himself was exceedingly delicate, and dependent on the most scrupulous care of his health. He was asthmatic, and subject to epilepsy. Sweating was his great panacea as he grew older, believing that one of the causes of the infirmities of age was due to the harder skin allowing less transpiration than the delicate skin of youth. Carrying out this theory, he himself took a heavy sweat every night, sleeping under four fur robes, so that some nights he had to change his linen as many as ten times. He also held that the aged ate too much, and himself often ate but one egg for his day's nourishment. By 1699 this regimen had reduced him to extreme feebleness. He began to have symptoms of stone in the bladder, which by 1701 could no longer be borne, and confined him to the bed. At last he was sounded by Mareschal, the diagnosis confirmed, and the old man of sixty-three came to the dreaded lithotomy. Refusing to be bound on the table, he declared he had ample control of himself to keep quiet, which he did through a long operation of perineal section, without any complaint or allowing a word to escape which showed suffering. He talked quietly with his surgeon during the operation; but when it was over and Mareschal gave some directions about his food, the old, first physician asserted himself at once and said, "I had great need, sir, of your hand; but I have none for your head to arrange my regimen of living." This retort gave great satisfaction to the physicians for many years.

It was the successful outcome of this operation which cemented the friendship of Fagon to Mareschal, and on the death of Felix, the first surgeon, shortly after, Fagon was very instrumental in having Mareschal appointed to the vacancy.

Fagon died in 1718. So far as we know, the only book he published was "A Treatise on the Qualities of Quinine," in 1703.

The life of George Mareschal, the first surgeon, reads like a romance. I will give you but the briefest outline to-night, for I hope later to write more fully the interesting story. He was as handsome as Fagon was ugly, as gracious as the first physician was crabbed; a man of wide tolerance, but inflexible on all questions affecting his honor or the advancement of his chosen profession.

The son of an emigrant Irish captain of cavalry under Louis XIII, he was born at Calais, April 8, 1658. His parents were both poor, and he was left a double orphan at the age of thirteen. He made his way to Paris, and obtaining a situation as a lad in a barbershop, hoped to obtain an education in surgery. He was unable to pay for full apprenticeship or for the examinations necessary to enter the guild of surgeons. His industry and determination, however, won him notice, and a happy friendship led to his obtaining a free house-officership in one of the convent hospitals. His skill and ability were marked, and he rapidly advanced; gained a mastership in the surgeons' guild of St. Côme, and became attending surgeon to the Charity Hospital. He developed great skill as a lithotomist, and rare judgment in his work, so that in 1696 he was called in consultation when Louis XIV was suffering from a large carbuncle, which the surgeons were failing to open sufficiently. His prompt insistence that they resort to radical incision doubtless saved the King's life, and brought Mareschal great credit at court, while his masterly diplomacy saved the reputation of the regular surgeons, and won their regard.

In 1703, Mareschal became first surgeon to the King, who, throughout the remainder of his life made not only a professional counsellor, but a close personal confidant of him—a trust which Mareschal amply justified. In 1707 he was ennobled by Louis, and became the Seigneur de Bièvre. He obtained the reversion of his office for his son Louis, and so high was the esteem in which he was held that on the wedding of this eldest son the marriage register was signed in person by every member of the royal family. After the death of Louis XIV Mareschal was reappointed first surgeon to the new King, Louis XV. To this appointment the good will of the Regent was of course essential, and though the Duke of Orleans was in every point of the opposite party to the late King, yet it was Mareschal, the King's surgeon, who had held out for a professional and non-political report on the autopsies of the royal princes in 1714, when rumor charged their deaths to poison, and practically alone, fully exonerated the Duke.

The great interest of Mareschal's life was the organization of surgical practice throughout the Kingdom, and freeing it from the domination of the physicians. Before he died he had succeeded, though with many a hard fight, in bringing all surgical study and license to practice under the sole jurisdiction and direct control of the first surgeon, who was made also ex-officio chief of surgery of the kingdom. This organization remained practically unchanged until the French Revolution wiped out every former system of the land.

He was made a Chevalier of the Order of St. Michael in 1723, and in 1732 founded the Royal Academy of Surgery, to whose proceedings he contributed some of the early papers.

He died December 13, 1736, possessed of large estates and ample fortune; held in high regard and affection by his colleagues as a man of character and unblemished reputation.

NOTES ON NEW BOOKS.

The Ocular Muscles: A Practical Handbook on the Muscular Anomalies of the Eye. By Howard F. Hansell, M. D., and Wendell Reber, M. D. Illustrated. $2.50. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This book is interesting, not so much for purposes of instruction as for setting forth in black and white the clinical views of the writers, who have devoted particular attention to the consideration of the eye muscles. Apparently they have been minute in their investigations, possibly too minute, especially in connecting bodily distresses of various sorts with Exophoria. "Out of 200 exophorics 140 gave a testimony of more or less vertigo." 70%! The reviewer confesses himself as not being in accord with a number of the ideas contained in this book, but the book covers a subject in which differences of opinion have for a long time existed. As a supplementary text-book for their own students this book may have a place, but for an impersonal exposition of the eye muscles and their anomalies, we would refer the student to other works. B. B. B., Jr.

The Treatment of Short-sight. By Professor Dr. J. Hirschberg. Translated by G. Lindsay Johnson, M. D. (*New York: Rebman Company, 1912.*)

This is rather an interesting little book on the subject of Myopia, not going into the subject exhaustively, but narrating the personal experiences of the author in this class of cases. The conclusions that the author reaches will probably meet with the approval and endorsement of most practicing oculists of experience. Some very useful and interesting statistic tables from Tscherning (p. 4), Donders (p. 13), Horner (p. 23), and the author's (pp. 23, 26, 59 and elsewhere) are included in the little book. B. B. B., Jr.

Untersuchungen ueber die Struktur der Blutzellen. Von Priv.-Doz. Dr. Alfred v. Decastello, Assistent, und Dr. Alexander Krjukoff, derzeit Hospitant der medizinischen Klinik in Innsbruck. $4.00. (*Berlin u. Wien: Urban & Schwarzenberg; New York: Rebman Company, 1911.*)

This monograph represents the result of a careful and painstaking study of the structure of the blood cells—a difficult subject. By the adoption of the most advanced methods of fixation and staining, preparations were made and then studied under the best available conditions—magnification up to 3000 times. The authors say that they frequently spent many hours in the examination of a single cell which was then carefully drawn. The splendid illustrations, 102 in number, included in the eight chromolithographic tables demonstrate the value of their study.

The results have not only brought out more clearly many known facts concerning the structure of the blood cell but have also pointed out new facts, as for instance: the demonstration of cells with tail like nuclei, amitotic division of splenocytes, and the occurrence of large complexes of erythrocytes in the circulating blood. The authors further conclude that the conception of the cell and the nucleus as a vesicle surrounded by a membrane is incorrect and that cell body as well as nucleus is composed of a tortuous matting of fibres which composes the greater portion of the cell. Nucleus and protoplasm do not represent anatomically and functionally distinct portions; they are closer related and nuclear fibres reach out into the protoplasm and become a part of the latter. The granules represent transformed segments of protoplasmic fibres. The blood platelets arise from the cytoplasm of leucocytes and show structural differences according to the type of cell from which they have arisen.

The above conclusions are of a great deal of interest. In many ways they differ from the accepted teachings, but it would lead too far to discuss these opinions in relation to the extensive recent hematological literature. It is to be regretted that the authors have included so little discussion of the literature in the presentation of their findings, which will limit the value of the volume.

Post-Mortems and Morbid Anatomy. By Theodore Shennan, M. D., F. R. C. S. 18/. (*London: Constable & Company, Limited, 1912.*)

This volume of 496 pages is intended by the author firstly to aid the student of medicine as well as the practitioner to intelligently conduct and report post mortem findings, and to assist the teacher in conveying clear pictures of the naked-eye appearances of diseased organs; secondly to aid and supplement the study of morbid anatomy by a brief discussion of the microscopical and bacteriological aspects of disease in as far as these are necessary for a clear comprehension of the naked eye appearances. Needless to say the field which the author has so well covered is a perilous and difficult one. Practical medicine can hardly be properly taught from text-books and the importance of first-hand information as regards pathological anatomy may not be emphasized too much.

The content of the book is divided into chapters arranged arbitrarily according to the methods employed at the Edinburgh Clinic. The numerous illustrations, 207 in number, compare favorably with those usually found in books of this nature. They are particularly adapted to illustrate gross anatomical changes such as, cardiac valvular stenoses, congenital anomalies and abnormalities of various organs, intestinal conditions as intussusception, ulcers of the intestine, abscesses, gummata, etc., of various organs, hydrocephalus, cerebral hemorrhage, etc., etc., but as usual fail completely in demonstrating more minute changes, such as fatty degeneration and fibroses of the myocardium, acute endocarditis, acute enteritis, the various changes in the nephritic kidney, etc. The two colored plates are good.

The portion of the appendix containing equivalent imperial and metrical measurements of weight, length and capacity, and laboratory methods of more general utility both for preserving tissues in their natural colors and for preparing microscopic sections, will be a handy aid to both student and practitioner laboratory workers. The utility of the portion containing the bibliography is hard to appreciate. It is necessarily incomplete, will rapidly become antedated and is hardly desirable with such catalogues of current literature as that of the Surgeon's General Library and the Index Medicus.

The book is written in a very agreeable style. Methods are clearly elucidated, and while one might take exception to the anatomical classification and description in a few instances, such as the inclusion of syphilitic aortitis simply as a type of endarteritis deformans, etc., the sketchy review of the pathological anatomy is in general very satisfactory.

The book should fill a considerable demand particularly in those schools where the post-mortem material is limited.

A Clinical Study of Acute Poliomyelitis. By Francis W. Peabody, M. D., George Draper, M. D., and A. R. Dochez, M. D. Monographs of the Rockefeller Institute for Medical Research, No. 4. (*New York: 1912.*)

This excellent monograph presents the results of careful investigations on 184 cases of acute poliomyelitis. The various phases of the disease are considered in some detail and the studies are preceded by an interesting history of poliomyelitis. The discussion of the symptomatology is of great interest and value.

This study should be in the hands of every student of infectious diseases who will derive genuine pleasure as well as profit from its reading.

International Clinics. Edited by Henry W. Cattell, M. D., and collaborators. Vol. III. 22d Series. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

The variety of lectures in each of these volumes makes them both entertaining and interesting to a large body of readers, for these so-called "Clinics" cover the whole field of medicine. This time we find papers on medical, surgical, ophthalmological and other subjects by such well known men as Solis-Cohen, Arthur Dean Bevan, Roberts, Deaver and others, and without further commendation it may be said that anything written by these men is worth reading.

Progressive Medicine: Edited by Hobart Amory Hare, M. D., etc., and Leighton F. Appleman, M. D., etc. Vol. III. Sept., 1912. (*Philadelphia and New York: Lea & Febiger.*)

The newer work in diseases of the thorax and its viscera, including the heart, lungs and bloodvessels, dermatology and syphilis, obstetrics, and diseases of the nervous system is reviewed in this volume, with the usual careful preparation by the contributing authors, Ewart, Gottheil, Davis and Spiller, all leaders in their special branches. For the busy practitioner *Progressive Medicine* is an important publication.

Manual of Chemistry. By W. Simon, M. D., and Daniel Base, Ph. D. Tenth Edition. Thoroughly Revised. Illustrated. (*Philadelphia and New York: Lea & Febiger, 1912.*)

We congratulate Dr. Simon on the appearance of the tenth edition of his *Chemistry*, which has proved itself so eminently satisfactory. The continued success of this work is due largely to the fact that the author keeps it up to date, and the student finds in it all the necessary newer information on the subjects discussed. It is one of the best of students' manuals.

London Practitioners' Manuals. Anæsthesia and Analgesia. By J. D. Mortimer, M. D., etc. $2. (*London: University of London Press, 1911.*)

Nothing new is presented in this book. As the author states in the preface it is a guide to the practitioner, the more scientific details being omitted. Special methods of anæsthesia are touched upon very lightly. The book is concise yet it contains a great many practical suggestions.

The chapters on "Duties and Responsibilities of the Anæsthetist," "Signs Indicating Depth of Anæsthesia," and "Dangers and Difficulties of Anæsthesia," are especially good. The description of the administration of N_2O and ethyl chloride is too meager to be of much value to one who has not already had considerable training. The discussion of percentage mixtures is interesting, especially the conclusion that "By far the most important factor in the safe administration of an anæsthetic is the experience of the administrator."

Further Researches Into Induced Cell-Reproduction and Cancer. Illustrated. The John Howard McFadden Researches. $1. (*London: John Murray, 1912.*)

This small volume is made up of four papers by H. C. Ross, J. W. Cropper and E. H. Ross. In these the writers show that "swellings resembling tumors" can be induced in animals "by the action of the same chemical substances which induce individual cell-multiplication." These substances they call "auxetics" and "augmentors." Workers along these and similar lines must need read these papers, which are not intended for the general practitioner but rather for the laboratory worker. The results obtained by Dr. Ross and his associates will have to be confirmed by others before they can be accepted as definite.

A Manual of Pharmacy for Physicians. By M. F. DeLorme, M. D. Third Edition. Illustrated. $1.25. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

For a certain class of students this manual may be sufficient, but it is not one to be recommended. It is elementary, and suited to those who have had but very little preliminary education before taking up the study of medicine. It is to be hoped that in a few years there will be no call for such works, which are an evidence of the low standards required by some American medical schools. In so far as it goes it serves its purpose satisfactorily.

Arteriosclerosis. By Louis M. Warfield, M. D. Illustrated. $2.50. (*St. Louis: C. V. Mosby Company, 1912.*)

Since the first appearance of this book four years ago Dr. Warfield has rewritten much of it, and added two important chapters on "The Physical Examination of the Heart and Arteries," and "Arteriosclerosis in Its Relation to Life Insurance." This is a useful work for the general practitioner and it is a satisfaction to note that a second edition was called for, since this is proof that this long little understood condition is now becoming more generally recognized by the doctors at large. They will find this volume really helpful.

Burdett's Hospitals and Charities—1912: The Year Book of Philanthropy and Hospital Manual. 10/6. (*London: The Scientific Press, Limited.*)

This volume furnishes all hospital superintendents with a large amount of valuable financial statistics, which, though conditions vary in different countries, are important from a comparative standpoint. In addition to the statistics there is much other general information which is serviceable. To Sir Henry Burdett, the editor, the improvement in the management of English hospitals is largely due, and this publication is the result of his efforts and energy. Unfortunately there is no similar work in this country, the need of one is great, for at present superintendents have no book to turn to where at a glance they can find the information about other hospitals in their own country all carefully compiled and edited.

The Kallikak Family: A Study on the Heredity of Feeble-Mindedness. By Henry Herbert Goddard, Ph. D. (*New York: The Macmillan Company, 1912.*)

Through the painstaking and laborious researches of Dr. Goddard and his assistants, this history of the Kallikak family is the most important one that exists as an exposition of the transmission of feeble-mindedness through many generations. What makes it of especial value is that there are two branches of the family both starting from the same ancestor. The one branch of feeble-minded began with the offspring of this ancestor and a feeble-minded girl; the other with the children by marriage of the ancestor with a healthy girl. The two branches never intermarried and can be traced to the present time, so that here it is possible to compare accurately, as has never been done before, the results which followed as a consequence of the union of a healthy man on the one hand with a feeble-minded woman, and on the other with a mentally normal woman. The study is of especial interest as confirming to some extent the Mendelian theory of heredity as applied to man, and also as an exposition of the calamitous results which are likely to follow the uniting of healthy and unhealthy stock. None can read this exposition

without being impressed by the need of state control of the feeble-minded and the benefits that will accrue if more attention is paid both to the physical and mental status of man and woman who contemplate matrimony. This is a most important contribution to the science of eugenics.

A Text-Book of Gynecology. By William S. Gardner, M. D. Illustrated. (*New York and London: D. Appleton & Co., 1912.*)

This little volume is an attempt to put the essentials of gynecology within easy reach of the busy medical student. It does not purport to be an exhaustive treatise, but the author's large experience as a teacher and intimate practical knowledge of his subject have enabled him to know just what to omit. He has shown excellent judgment in this respect and has succeeded admirably in the difficult undertaking of producing a brief treatise that is, nevertheless, clear, readable, and sufficiently comprehensive to meet the actual needs of all students except those especially interested in this field of surgery. The pathological side of the subject has received noteworthy attention, the photomicrographs being particularly good. The book will undoubtedly become a general favorite with medical students, for its teaching is eminently sound and practical.

E. H. R.

The Therapy of Syphilis: Its Development and Present Position. By Dr. Paul Mulzer, Berlin, with a preface by Prof. P. Uhlenhuth, M. D. Translated by A. Newbold. $1.50. (*New York: Rebman Company.*)

This work, though giving some consideration to other methods of treatment, is chiefly concerned with salversan therapy from the point of view of the practitioner. The historical development of the use of arsenic compounds in spirochætal infections is traced in an interesting manner, especial attention being given to the experimental work on which it is based. Various methods of administration are well described. The early results of the clinical use of salversan are given in detail, but as these are only carried to the close of the year 1910, from the present standpoint they are very incomplete. The language in the translation is involved, and in places the meaning is obscure. While the original work at the time of its first appearance served its purpose well, it has already become so old as to have lost much of its usefulness.

P. W. C.

The Wassermann Reaction: Its Technique and Practical Application in the Diagnosis of Syphilis. By John W. Marchildon, M. D. $1.50. (*St. Louis: C. V. Mosby Company, 1912.*)

This book is evidently written as a laboratory manual for those who have had little or no training in laboratory work. It contains very little that is new or original. It gives in profuse detail the various steps in carrying out the reaction, following for the most part the original method of Wasserman. Recent modifications of the reaction, in particular that of Noguchi, receive scanty consideration.

P. W. C.

Recent Studies of Syphilis. A reprint of articles published in the *Interstate Medical Journal.* Second Edition (revised), Sept., 1911. (*St. Louis: Interstate Medical Journal Company.*)

This is an interesting collection of special articles dealing with various phases of the subject. Laboratory diagnostic methods are well described, especially Noguchi's modification of the Wassermann reaction. Of especial interest are the articles dealing with salvarsan therapy. The conservative attitude taken as to the use of the drug and the probability of permanent cure is to be commended. It should be of real use to those engaged in the treatment of syphilis, and especially to the general practitioner.

P. W. C.

Auto-Intoxication and Disintoxication: An Account of a New Fasting Treatment in Diabetes and Other Chronic Diseases. By Dr. G. Guelpa (Paris). Translated by F. S. Arnold, M. B. $1.25. (*New York: Rebman Company, 1912.*)

Not so many years ago it was a common practice for parents to purge their children actively every spring and doubtless this old domestic method of treatment had distinct advantages in many instances. Dr. Guelpa advocates a purge and fasting of two or three days for many patients suffering from chronic affections of one sort or another, and says they derive great benefit from it. This is more than likely and it is probable that many suffer because they do not get their intestines ever properly cleared, that there is always some residue. Occasional fasting such as recommended by the author has its merits also. Dr. Jones, of New York, has long advocated violent purging in severe chronic rheumatic conditions, and many patients have benefited by this method of "disintoxication" as it is named by Dr. Guelpa. In advocacy of his treatment he, however, has such strange theories, that it is impossible to do more than bring to the attention of the profession the value that often lies in an active purge and an absention from all food except liquids for a day or two in various affections.

The Pituitary Body and Its Disorders. By Harvey Cushing, M. D. Illustrated. $4. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

Dr. Cushing has devoted the greater part of his time and energies, during the past four years, to the experimental and clinical study of the pituitary body, and this book, in which his experiences are admirably set forth, is of equal interest for the physiologist, the internist, the surgeon, the neurologist and the ophthalmologist.

The book contains many valuable contributions to physiology. Especially interesting in this connection are the observations on the inter-relations of the ductless glands; the influence exerted by the hypophysis on carbohydrate metabolism; and the experiments on feeding and transplanting glands as a therapeutic measure in hypo-pituitarism.

The clinical symptoms of the various pituitary disorders—gigantism, acromegaly, and the symptom complex resulting from a deficient secretion—are discussed in great detail. There are numerous photographs showing the general appearance of patients of each of these groups; also reproductions of the X-rays of the more interesting cases. To many of the case reports are appended a series of carefully made perimetric charts, showing the changes in the form of the visual fields before and after operative therapy.

We regard this book as the most important of the contributions to this subject in English, or indeed in any language. The reading matter is concise and to the point. The illustrations are good. Pituitary disorders are scarcely less frequent than are those of the thyroid; and after reading this book many practitioners will realize that they have had, at one time or another, similar cases under their care.

A Practical Treatise on Fractures and Dislocations. By Louis A. Stimson, M. D., etc. Seventh Edition. Revised and Enlarged. Illustrated. (*New York and Philadelphia: Lea & Febiger, 1912.*)

Stimson's work has received such world-wide recognition, and its admirable qualities have been so abundantly recognized by

both teachers and students, that it needs no new word of commendation from us. A few sections on some of the less frequent fractures have been added and new photographs, making the new edition more complete than any of its predecessors. It is a pleasure to note the success of this work, which will long remain one of the best American surgeries.

The Healthy Baby. By ROGER H. DENNETT, M. D. $1.00. (*New York: Macmillan Company, 1912.*)

This book has been written to assist inexperienced mothers. It aims especially to describe the "everyday care" required by a healthy child but the common ailments of infancy also receive the attention they merit. The author explains the value of the doctor's advice and discusses the signs of illness which should lead the mother to consult him. The book covers the whole period of infancy, including everything the young mother should know from the time her baby is born until it is two or three years old. The information is accurate; the style is clear and simple. In addition to a full index, marginal headings are provided which make reference easy.

A Manual of Surgical Treatment. By SIR W. WATSON CHEYNE, Bart., F. R. S., etc., and F. F. BURGHARD, F. R. C. S. Vol. III. (*Philadelphia and New York: Lea & Febiger, 1912.*)

This is the third volume of the revised edition of Cheyne and Burghard's well known manual. Drs. Legg and Edmunds have done their work of revision thoroughly and they have rewritten many parts. This edition corresponds to the first in being in five volumes, and in this one is contained the treatment of the surgical affections of the joints, the spine, the head, and the face. It is well illustrated, and a student or doctor who can afford to buy this manual will find it profitable, but there are so many surgeries in single volumes and in systems of many volumes that it is most difficult to make a choice, it is an embarrassment of riches. This is an excellent guide, however, and as a surgeon should make himself acquainted with foreign methods as well as those of his own land, he cannot do better than study Cheyne and Burghard.

Making Good on Private Duty: Practical Hints to Graduate Nurses. By HARRIET CAMP LOUNSBERY, R. N. $1.00. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

These hints have already appeared in large part in one or two of the nursing journals, and it was hardly worth while to republish them in book form. If a nurse, before she graduated, had not been taught these primary principles, she certainly would not be fit to commence her career as a private nurse. There are one or two brief chapters which may prove helpful to any nurse, but those on conduct are so elementary as to be almost laughable; and "Making Good on Private Duty" is not essential to a nurse's stock of books on her own profession.

A Clinical Manual of the Malformations and Congenital Diseases of the Fœtus. By PROFESSOR DR. R. BIRNBAUM. Translated and Annotated by G. BLACKER, M. D., etc. (*Philadelphia: P. Blakiston's Son & Co., 1912.*)

This work is one of large interest to the physician and surgeon as well as the obstetrician, who sees these malformations more often than any other class of practitioner. Dr. Birnbaum has not attempted to write a complete treatise on the subject since this would have necessitated a much larger work, but he has described those malformations which are of more general interest to the surgeon, and on the other hand from the medical point of view has omitted such diseases as congenital syphilis, congenital infectious diseases, and asphyxia neonatorum, as all these are commonly fully described in the text-books on children's diseases. For the general practitioner he has compiled a large amount of valuable information which is only to be found scattered throughout the literature and has produced a work which will be of real service to a large body of doctors. There is none other in English which can be compared with it as a practical discussion of the subject, though there is an immense literature on teratology.

The Practitioner's Visiting List for 1913. A pocket-sized book containing memoranda and data important for every physician, and ruled blanks for recording every detail of practice. The Weekly, Monthly and 30-Patient Perpetual contain 32 pages of data and 160 pages of classified blanks. The 60-Patient Perpetual consists of 256 pages of blanks alone. Each in one wallet-shaped book, bound in flexible leather, with flap and pocket, pencil with rubber, and calendar for two years. Price by mail, postpaid, to any address, $1.25. Thumb-letter index, 25 cents extra. (*Philadelphia and New York: Lea & Febiger, Publishers.*)

The above description, taken from the publishers' circular, describes the pocket book. Many such pocket books are annually produced, all very similar in character, and we are glad to call attention to them, as they evidently are serviceable to a large body of practitioners.

Lehrbuch der Augenheilkunde in der Form Klinischer Besprechungen. Von DR. PAUL RÖMER. Illustrirt. Mks. 22.50. (*Berlin u. Wien: Urban & Schwarzenberg. New York: Rebman Company, 1910.*)

This would be found a most excellent text-book to recommend to students on the eye were it not for the fact that the fact that the subject matter is presented in the form of clinical lectures which of necessity requires excessive verbiage. The author describes the various diseases of the eye with wonderful preciseness and he lays particular stress on a correct understanding of the anatomical and pathological changes which the diseased eyes undergo as a basis for rational therapeusis. Clear mental pictures are thus given the reader, and there are reasons and explanations in detail for all the clinical factors involved. Without further criticism, for we can only say that it is an excellent text-book, and may be studied and read with profit, we wish to call particular attention to the very exhaustive consideration of the lens of the eye. This subject matter which comprises Part 4 of the present volume is the most complete and masterly monograph on the "Lens" which we know of, and the author shows therein marvelous skill in presenting the most recent work of others, enriched with observations and explanations of his own which are most satisfactory. For instance the nutrition of the lens has long been considered a matter of speculation, but the present author shows that the recent work of Rissling, Leber, Hess, and himself has put so many demonstrable facts at our disposal as to render this part of the eye almost independent of fancy.

In no part of the present work is the subject matter compressed and yet one would not go far wrong should he consider every page as worthy of his close attention and memory.

B. B. B., JR.

Text-Book of Ophthalmology in the Form of Clinical Lectures. By DR. PAUL RÖMER. Translated by DR. MATTHIAS LANCKTON FOSTER. Illustrated. Vol. I. (*New York: Rebman Company, 1912.*)

This is merely the translation in part of the work reviewed above. The work of the translator has been done conscientiously and well, and it is fortunate that Römer's masterly work can be had by those who only read English.

Man's Redemption of Man: A Lay Sermon. By William Osler. 50cts. (*New York: Paul B. Hoeber, 1912.*)

In neat pocket form it is a pleasure to welcome anew this delightful essay, already familiar to all admirers of the author. It is an essay all young students of medicine should read and ponder over, and the more familiar it becomes to the profession, the higher will grow its aspirations and ideals.

Oxford Medical Publications: Tuberculin Treatment. By Clive Riviere, M. D., and Egbert Moreland, M. D. $2.00. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

This volume, without entering deeply into the scientific basis and data of tuberculin therapy, will yet serve well as a practical hand-book for those wishing to acquire a technique. The diagrams, though often based on much that is assumption, help to point many a tuberculin moral. Worthy of note is the emphasis laid upon the dual anti-body system that is apparently concerned with tuberculin hypersensitiveness. Taking time entirely too much by the forelock, is the assignment of a large section of the book to the treatment of certain forms of tuberculosis by the method of persistently small doses. Not that such treatment may not be gracefully advocated, but the advocacy is too strong for our task when it supports itself upon a classification of tuberculous diseases framed as much to fit the occasion as with thought to its ulterior justification. In other respects, the book is eminently clear and sane, and is to be welcomed as a contribution to a subject which is being more and more discussed. S. W.

1. *A Text-Book of Obstetrics: Including Related Gynecologic Operations.* By Barton Cooke Hirst, M. D. Seventh Revised Edition. Illustrated. $.500. *1912.*
2. *A Text-Book on the Practice of Gynecology.* For Practitioners and Students. By W. Easterly Ashton, M. D. Fifth Edition, Thoroughly Revised. Illustrated. $6.50. *1912.*
3. *A Text-Book Upon the Pathogenic Bacteria and Protozoa.* For Students of Medicine and Physicians. By Joseph McFarland, M. D. Seventh Edition, Thoroughly Revised. Illustrated. $3.50. *1912.*
4. *Diseases of the Stomach, Intestines and Pancreas.* By Robert Coleman Kemp, M. D. Second Edition, Revised and Enlarged. Illustrated. $6.50. *1912.*

From the publishers, W. B. Saunders Company, we have received the last editions of the four above-named works. The fact that there is a constant demand by the profession for these books indicates how well the authors have met the needs of students and practitioners. All the volumes show some alterations which add to their usefulness. It is a satisfaction to note that there is a call for these reliable and well written books. Both authors and publishers are to be congratulated on their success.

BOOKS RECEIVED.

Oxford Medical Publications. Henry Frowde, London; Hodder & Stoughton, London.

1. *X-Ray Diagnosis and Treatment.* By W. J. S. Bythell, B. A. Cantab., M. D. Vict., and A. E. Barclay, M. D. Cantab., M. R. C. S., L. R. C. P. 1912. 8vo. 147 pages.
2. *Consumption in General Practice.* By H. Hyslop Thomson, M. D., D. P. H. 1912. 8vo. 335 pages.
3. *Surgery of the Rectum for Practitioners.* By Sir Frederick Wallis, M. B., B. C. Cantab., F. R. C. S. 1912. 8vo. 355 pages.
4. *The Practitioner's Encyclopædia of Medicine and Surgery.* In all their Branches. Edited by J. Keogh Murphy, M. C. (Cantab.), F. R. C. S. 1912. 4to. 1423 pages.

The Mechanistic Conception of Life. Biological Essays. By Jacques Loeb, M. D., Ph. D., Sc. D. 1912. 8vo. 232 pages. The University of Chicago Press, Chicago, Illinois.

Practical Anatomy. An Exposition of the Facts of Gross Anatomy from the Topographical Standpoint and a Guide to the Dissection of the Human Body. By John C. Heisler, M. D. With 366 illustrations, of which 225 are in color. By E. F. Faber. [1912.] 8vo. 790 pages. J. B. Lippincott Company, Philadelphia and London.

Pharmacology and Therapeutics. By Horatio C. Wood, Jr., M. D. 1912. 8vo. 429 pages. J. B. Lippincott Company, Philadelphia and London.

The Pituitary Body and Its Disorders. Clinical States Produced by Disorders of the Hypophysis Cerebri. By Harvey Cushing, M. D. An Amplification of the Harvey Lecture for December, 1910. 319 Illustrations. 1912. 8vo. 341 pages. J. B. Lippincott Company, Philadelphia and London.

A Text-Book of Obstetrics. By Barton Cooke Hirst, M. D. Seventh edition, revised and enlarged with 895 illustrations, 53 of them in colors. 1912. 8°. 1013 pages. W. B. Saunders Company, Philadelphia and London.

A Text-Book on the Practice of Gynecology. By William Easterly Ashton, M. D., LL. D. With ten hundred and fifty new line drawings illustrating the text by John V. Alteneder. Fifth edition, thoroughly revised. 1912. 8°. 1100 pages. W. B. Saunders Company, Philadelphia and London.

Arteriosclerosis, Etiology, Pathology, Diagnosis, Prognosis, Prophylaxis, and Treatment. With a special chapter on Blood Pressure. By Louis M. Warfield, A. B., M. D. With an introduction. By W. S. Thayer, M. D. Illustrated with twenty-eight engravings. 1912. 8vo. 220 pages. C. V. Mosby Company, St. Louis.

Principles of Microbiology. A Treatise on Bacteria, Fungi and Protozoa Pathogenic for Domesticated Animals. By Veranus Alva Moore, B. S., M. D., V. M. D. One hundred and one illustrations. 1912. 8vo. 506 pages. Carpenter and Company, Ithaca, New York.

A Text-Book of Practical Therapeutics. With Especial Reference to the Application of Remedial Measures to Disease and their Employment upon a Rational Basis. By Hobart Amory Hare, M. D., B. Sc. Fourteenth edition, enlarged, thoroughly revised, and largely rewritten. Illustrated with 131 engravings and 8 plates. 1912. 8vo. 984 pages. Lea & Febiger, Philadelphia and New York.

Pharmacology: Action and Uses of Drugs. By Maurice Vejux Tyrode, M. D. Second edition. 1912. 8vo. 288 pages. P. Blakiston's Son & Co., Philadelphia.

Philadelphia General Hospital Reports. Volume VIII. 1910. Edited by David Riesman, M. D. 1911. 8vo. 367 pages. Dunlap Printing Co., Philadelphia.

Fifth Scientific Report on the Investigations of the Imperial Cancer Research Fund. Under the Direction of the Royal College of Physicians of London and the Royal College of Surgeons of England. By Dr. E. F. Bashford. 1912. 8vo. 94 pages. Taylor and Francis, London.

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